

**UCLA**

**UCLA Electronic Theses and Dissertations**

**Title**

Early Family Stress, Biobehavioral and Psychosocial Functioning, and Inflammation

**Permalink**

<https://escholarship.org/uc/item/00m9f9nq>

**Author**

Chiang, Jessica

**Publication Date**

2016

Peer reviewed|Thesis/dissertation

UNIVERSITY OF CALIFORNIA

Los Angeles

Early Family Stress, Biobehavioral and Psychosocial Functioning, and Inflammation

A dissertation submitted in partial satisfaction of the requirements for the degree

Doctor of Philosophy in Psychology

by

Jessica Chiang

2016



## ABSTRACT OF THE DISSERTATION

Early Family Stress, Biobehavioral and Psychosocial Functioning, and Inflammation

by

Jessica Chiang

Doctor of Philosophy in Psychology

University of California, Los Angeles, 2016

Professor Andrew J. Fuligni, Co-Chair

Professor Shelley E. Taylor, Co-Chair

Family stress such as conflict, abuse, neglect, or insensitive parenting, experienced in early life during childhood and adolescence increases risk for adverse health outcomes. Heightened inflammation is thought to be a key pathway by which early family stress increases risk for poor health. Studies have established a link between early family adversity and inflammation, and theoretical models posit several mechanisms linking early family stress to inflammation, including disruptions in biological stress systems (i.e., altered hypothalamic-pituitary-adrenal (HPA) axis and heightened sympathetic nervous system responses to stress) and psychosocial functioning (i.e., higher threat appraisals, heightened emotional reactivity to stress, poorer social relationships). Empirical studies also suggest that disrupted sleep may be an important pathway. The current study tests these putative pathways in a single study, which has been relatively uncommon in prior research. Participants were 91 late adolescents from Latino

and European-Americans backgrounds. Participants completed the Trier Social Stress Test (TSST), a well-validated, widely used laboratory-based acute social stressor, and completed questionnaires assessing their family environment from childhood through mid-adolescence. They provided blood and saliva samples for the assessment of their inflammatory, hypothalamic-pituitary-adrenal axis, and sympathetic nervous system responses to the TSST. Additionally, they completed questionnaires assessing their sleep, cognitive appraisals of the stress task, their emotional responses to the TSST, and their current social relationships. Results showed that growing up in a stressful family environment was not related to heightened inflammatory responses to the TSST. However, late adolescents who grew up in a stressful family environment exhibited dampened cortisol responses to the TSST, poorer sleep, heightened threat appraisals, lower emotional reactivity, and poorer social relationships. In turn, dampened cortisol responses were associated with greater increases in inflammation across the laboratory session. Heightened threat appraisals, lower emotional reactivity, and more supportive social relationships were related to attenuated cortisol responses. Together, these findings suggest that early family stress impacts HPA-axis responses to stress, sleep, and psychosocial functioning, but that these in turn, may have little impact on inflammatory responses to stress, at least during late adolescence.

The dissertation of Jessica Chiang is approved.

Julienne Elizabeth Bower

Teresa Ellen Seeman

Andrew J. Fuligni, Committee Co-Chair

Shelley E. Taylor, Committee Co-Chair

University of California, Los Angeles

2016

Dedicated to my family and spouse.

## TABLE OF CONTENTS

|      |                                                                                                  |    |
|------|--------------------------------------------------------------------------------------------------|----|
| I.   | Introduction.....                                                                                | 1  |
|      | A. Early Adversity and Inflammation.....                                                         | 2  |
|      | B. Biological Pathways: HPA Axis, SNS, and Sleep.....                                            | 5  |
|      | C. Psychosocial Pathways: Cognitive Appraisal, Emotion Reactivity, and Social Relationships..... | 11 |
|      | D. Current Study.....                                                                            | 17 |
| II.  | Methods.....                                                                                     | 22 |
|      | A. Participants.....                                                                             | 22 |
|      | B. Procedure .....                                                                               | 23 |
|      | C. Measures .....                                                                                | 25 |
|      | D. Statistical Analysis .....                                                                    | 32 |
| III. | Results.....                                                                                     | 34 |
|      | A. Descriptive Statistics.....                                                                   | 34 |
|      | B. Manipulation Check.....                                                                       | 35 |
|      | C. Early Adversity and Inflammation.....                                                         | 36 |
|      | D. Early Family Stress, Biobehavioral Processes, and Inflammation .....                          | 37 |
|      | E. Early Family Stress, Psychosocial Processes, and Inflammation .....                           | 42 |
|      | F. Psychosocial Functioning and HPA axis and sAA Responses to Stress .....                       | 44 |
|      | G. Gender, Ethnicity, and Subtypes of Early Family Stress.....                                   | 47 |
| IV.  | Discussion.....                                                                                  | 49 |
| V.   | Tables.....                                                                                      | 70 |
| VI.  | Figures.....                                                                                     | 86 |
| VII. | References.....                                                                                  | 96 |

## LIST OF TABLES

|           |                                                                                                                       |    |
|-----------|-----------------------------------------------------------------------------------------------------------------------|----|
| Table 1.  | Descriptives of Study Variables.....                                                                                  | 70 |
| Table 2a. | Bivariate Correlations between Early Family Stress, Inflammatory Reactivity, and Control Variables.....               | 73 |
| Table 2b. | Bivariate Correlations between Early Family Stress, Inflammatory Reactivity, Control, and HPA and SNS Variables.....  | 74 |
| Table 2c. | Bivariate Correlations between Early Family Stress, Inflammatory Reactivity, Control, and Sleep Variables.....        | 75 |
| Table 2d. | Bivariate Correlations between Early Family Stress, Inflammatory Reactivity, Control, and Psychosocial Variables..... | 76 |
| Table 3.  | Multilevel Growth Curve Model Predicting IL-6 from Early Family Stress x Time.....                                    | 78 |
| Table 4.  | Multilevel Growth Curve Model Predicting Cortisol from Early Family Stress x Time.....                                | 79 |
| Table 5.  | Multilevel Growth Curve Model Predicting IL-6 from Cortisol AUC <sub>i</sub> x Time....                               | 80 |
| Table 6.  | Multilevel Growth Curve Model Predicting sAA from Early Family Stress x Time.....                                     | 81 |
| Table 7.  | Multiple Regression Models Predicting PSQI Sleep Variables from Early Family Stress.....                              | 82 |
| Table 8.  | Multiple Regression Models Predicting Threat Appraisals from Early Family Stress.....                                 | 83 |
| Table 9.  | Multiple Regression Models Predicting Emotional Reactivity from Early Family Stress.....                              | 84 |
| Table 10. | Multiple Regression Models Predicting Supportive Relationships from Early Family Stress .....                         | 85 |

## LIST OF FIGURES

|             |                                                                                                                                                                    |    |
|-------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------|----|
| Figure 1.   | Experimental session timeline.....                                                                                                                                 | 86 |
| Figure 2a.  | IL-6 increased from 30 to 90 minutes post-TSST across the study sample.....                                                                                        | 87 |
| Figure 2b.  | Cortisol peaked 30 minutes post-TSST across the study sample.....                                                                                                  | 87 |
| Figure 2c.  | sAA peaked 30 minutes post-TSST across the study sample.....                                                                                                       | 87 |
| Figure 3.   | IL-6 slopes did not differ between individuals who experienced low levels of early family stress and those who experienced high levels of early family stress..... | 88 |
| Figure 4.   | Individuals who experienced high levels of early family stress exhibited dampened cortisol responses to the TSST.....                                              | 89 |
| Figure 5a.  | There was an accelerated increase in IL-6 for individuals with lower cortisol AUCi. ....                                                                           | 90 |
| Figure 5b.  | There was an accelerated increase in IL-6 for individuals with lower cortisol reactivity (change scores). ....                                                     | 90 |
| Figure 5c.  | There was an accelerated increase in IL-6 for individuals with slower recovery. ....                                                                               | 90 |
| Figure 6.   | sAA responses to the TSST did not differ between individuals of high and low levels of early family stress. ....                                                   | 91 |
| Figure 7.   | There was an accelerated increase in IL-6 for individuals with shorter sleep latency, but the change in slopes was due to higher levels of baseline IL-6.....      | 92 |
| Figure 8a.  | Cortisol responses were attenuated for individuals with higher anticipatory threat appraisals compared to those with lower anticipatory threat appraisals...       | 93 |
| Figure 8b.  | Cortisol responses were attenuated for individuals with higher retrospective threat appraisals compared to those with lower retrospective threat appraisals..      | 93 |
| Figure 9a.  | Cortisol responses were heightened for individuals with high NA reactivity compared to individuals with low NA reactivity.....                                     | 94 |
| Figure 9b.  | Cortisol responses were heightened for individuals with high fear reactivity compared to individuals with low fear reactivity.....                                 | 94 |
| Figure 9c.  | Cortisol responses were heightened for individuals with high guilt reactivity compared to individuals with low guilt reactivity.....                               | 94 |
| Figure 10a. | Cortisol responses were attenuated for individuals with less emotional closeness compared to individuals with more emotional closeness.....                        | 95 |
| Figure 10b. | Cortisol responses were attenuated for individuals with less tangible support compared to individuals with more tangible support.....                              | 95 |

## ACKNOWLEDGEMENTS

This project was supported by funding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (R01-HD062547), UCLA California Center for Population Research funded by the National Institute of Child Health and Human Development (R24-HD041022), UCLA Older Americans Independence Center funded by the National Institute of Aging (P30-AG028748), UCLA Cousins Center for Psychoneuroimmunology, University of California Institute for Mexico and the US, American Psychological Association, and Division 38 of the American Psychological Association. This project was also made possible through fellowship support from a Philip & Aida Siff Educational Foundation Scholarship, Ursula Mandel Scholarship, Edwin W. Pauley Fellowship, and Dissertation Year Fellowship from the UCLA Graduate Division.

Thank you to my doctoral committee for their valuable guidance on this project. I am especially grateful to my advisors Drs. Andrew Fuligni, Julie Bower, and Shelley Taylor for their unwavering dedication and commitment to my intellectual growth. I am humbled by their knowledge, generosity, and sincerity, and fortunate to have received their mentorship.

Many thanks to research assistants Ahra Ko, Melissa Gussman, Jessica Jedvaj, Tiffany Kwok, Danielle Arbios, Sabrina Jiang, Chelsea Revel, Madison Lyon, Tyson Kerr, Nick Herzog, Anna Shanazari, Camila Reyes, Asra Khan, Alex Aiello, Sammy Jamal, and Lucas Ferreira. This work would not have been possible without them.

Lastly, many, many thanks to God for His grace and countless blessings. My deepest gratitude to my parents Sharn and Catherine Chiang, siblings, Claire and David Chiang, and partner in life, Adam Hong, for their unconditional love and support, and for keeping me grounded and sane.

## VITA

### EDUCATION

- 2011 M.A. University of California, Los Angeles  
Major: Health Psychology  
Master's Thesis: Negative and Competitive Social Interactions are Related to Heightened Pro-inflammatory Cytokine Activity
- 2007 B.A. Smith College  
Majors: Psychology and Economics  
Honors: Magna Cum Laude, Phi Beta Kappa, First Group Scholars, Dean's List

### HONORS AND AWARDS

- 2015 Dissertation Year Fellowship, UCLA Graduate Division (\$20,000)
- 2015 Ursula Mandel Scholarship (\$15,000)
- 2014 Philip & Aida Siff Educational Foundation Scholarship (\$5,000)
- 2014 American Psychological Association Dissertation Research Award (\$1,000)
- 2014 American Psychological Association Division 38 Graduate Student Research Award (\$1,500)
- 2014 American Psychosomatic Society Young Scholars Award (\$500)
- 2013 UCLA Health Psychology Graduate Student Paper Prize (\$100)
- 2013 APA Basic Psychological Science Research Grant Honorable Mention
- 2012 Association for Psychological Science Student Travel Award (\$200)
- 2011 Graduate Summer Research Mentorship Fellowship, UCLA Graduate Division (\$4,700)
- 2011 National Science Foundation Graduate Fellowship (\$32,000)
- 2010 Edwin W. Pauley Fellowship, UCLA Graduate Division (\$20,000)

### GRANTS

- 2015- University of California Institute for Mexico and the US (\$11,900)
- 2016 *Understanding disease risk among Mexicans in the U.S.: The impact of early family stress on inflammation and underlying mechanisms.*
- 2014- UCLA Cousins Center for Psychoneuroimmunology (\$40,000)
- 2016 *Early family stress and inflammation: Underlying biological and psychosocial mechanisms.*
- 2014 UCLA Clinical & Translational Research Center (\$6,000)  
*Early family stress and inflammation: Underlying biological and psychosocial mechanisms.*
- 2011 UCLA Center for Culture, Brain, & Development (\$6,000)  
*The role of culture in the psychological and physiological effects of self-reflection over a stressor.*

## PUBLICATIONS

- Guan, A. S., **Chiang, J. J.**, Sherman, L., & Robles, T. (under review). Social support across context during young adulthood.
- Huynh, V. W. & **Chiang, J. J.** (in press). Subjective social status and adolescent health: The role of stress and sleep. *Youth & Society*.
- Chiang, J. J.**, Tsai K. M., Park, H., Bower, J. E., Almeida, A. M., Dahl, R. E., Irwin, M. R., Seeman, T. E., & Fuligni, A. J. (2016). Family stress and HPA functioning during adolescence: The moderating role of sleep. *Psychoneuroendocrinology*, 71, 43-53.
- Tsai, W., **Chiang, J. J.**, & Lau, A. S. (2016). The effects of self-enhancement and self-improvement on recovery from stress differ across cultural groups. *Social Psychological and Personality Science*, 7(1), 21-28.
- Chiang, J. J.**, Taylor, S. E., & Bower, J. E. (2015). Early adversity, neural development, and inflammation. *Developmental Psychobiology*, 57(8), 887-907.
- Chiang, J. J.**, Almeida, D. M., Bower, J. E., Seeman, T. E., Irwin, M., & Fuligni, A. J. (2015). Socioeconomic status, daily affective and social experiences, and inflammation during adolescence. *Psychosomatic Medicine*, 77(3), 256-266.
- Ortiz Parada, M., Wiley, J., & **Chiang, J. J.** (2014). How stress gets under the skin o como el estrés psicológico se introduce bajo la piel. *Revista Medica de Chile*, 142, 767-774.
- Chiang, J. J.**, Saphire-Bernstein, S., Kim, H. S., Sherman, D. K., & Taylor, S. E. (2013). Cultural differences in the link between supportive relationships and proinflammatory cytokines. *Social Psychological and Personality Science*, 4(5), 511-520.
- Chiang, J. J.**, Eisenberger, N. I., Seeman, T. E., & Taylor, S. E. (2012). Negative and competitive social interactions are related to heightened proinflammatory cytokine activity. *Proceedings of the National Academy of Sciences*, 109, 1878-1882.
- Jackson, B., Twenge, J. M., Souza, C., **Chiang, J.**, & Goodman, E. (2011). Low social status promotes ruminative coping. *Journal of Applied Social Psychology*, 41(10), 2434-2456.

## SELECTED CONFERENCE PRESENTATIONS

- Guan, S. S. A., **Chiang, J.**, Sherman, L. E., Nguyen, J., Tsui, Y., & Robles, T. (October, 2016). *Computer mediated communication and well-being*. Conference flash talk, Society for Research on Child Development Special Topic Meeting: Technology and Media in Children's Development, Irvine, CA.
- Chiang, J.**, Tsai, K. M., Park, H., Bower, J. E., Almeida, D. M., Dahl, R. E., Irwin, M. R., Seeman, T. E., & Fuligni, A. J. (March, 2015). *Family demands, sleep, and HPA-axis functioning among adolescents*. Conference symposium, Society for Research on Adolescence, Baltimore, MD.
- Chiang, J.**, & Fuligni, A. J. (March, 2014). *Does socioeconomic status affect daily socioemotional experiences to impact adolescent health?* Conference paper oral presentation, American Psychosomatic Society, San Francisco, CA.

## **Introduction**

The family context is crucial to youth development and long-term health. Family-related stress – including conflict, abuse, neglect, socioeconomic disadvantage, parental psychopathology, parental loss, and insensitive or cold parenting – experienced during childhood and adolescence increase risk for depression, obesity, lung disease, cancer, heart disease, and diabetes (Felitti et al., 1998; Miller, Chen, & Parker, 2011; Norman et al., 2012; Repetti, Taylor, & Seeman, 2002). Although the link between early family stress and poor health is robust and well-established, underlying mechanisms remain incompletely understood. One potential pathway that has received increasing attention is inflammation (Fagundes, Glaser, & Kiecolt-Glaser, 2013; Miller, et al., 2011).

Inflammation is a natural, early response of the immune system to pathogens and injured tissue. In response to damaged tissue or infection, immune communication molecules known as pro-inflammatory cytokines facilitate clearance of the pathogen and injured tissue from the body and promote repair. As such, inflammation is essential to healing and survival. However, prolonged or exaggerated inflammatory responses inflammation can result in chronic inflammation, a state implicated in depression, hypertension, obesity, diabetes, atherosclerosis, cardiovascular disease, and some cancers (Aggarwal, 2010; Libby, 2006; Medzhitov, 2010; Niskanen et al., 2004; Pauletto & Rattazzi, 2006; Raison, Capuron, & Miller, 2006; Wellen & Hotamisligil, 2005).

Past studies indicate higher levels of inflammation among individuals experiencing early adversity. However, past studies have focused primarily on adults with little work focusing on youth. Additionally, past studies have relied on baseline levels of inflammation with few studies assessing inflammatory reactivity despite that heightened reactivity may be a key mechanism that leads to chronic inflammation over time. Furthermore, although theoretical models posit

biological and psychosocial pathways linking early family stress to heightened inflammation and poor health, few studies have tested these pathways in a single study. As such, we do not completely understand how early family stress leads to low-grade chronic inflammation that increases risk for developing chronic diseases. To address these gaps, the present study examined how early family adversity affects inflammatory reactivity and evaluated the underlying physiological and psychosocial mechanisms.

### **Early Adversity and Inflammation**

Past studies have revealed a positive association between early family adversity and circulating markers of inflammation in adulthood. For instance, adults who were raised in a cold, conflictual family environment or experienced child maltreatment (i.e., physical abuse, sexual abuse, changes in caregiver, harsh discipline, and maternal rejection) before age 12 have been shown to have greater levels of C-reactive protein (CRP), a marker of systemic inflammation, as demonstrated cross-sectionally (S. E. Taylor, Lehman, Kiefe, & Seeman, 2006) and longitudinally (Danese, Pariante, Caspi, Taylor, & Poulton, 2007). In one prospective study, mothers reported whether their children experienced any socially adverse events (i.e., taken into foster care, physically hurt by someone, sexually abused, separated from either parent) in the previous 12-18 months every year for the first eight years of their children's lives. Children's levels of interleukin (IL)-6, a pro-inflammatory molecule, and CRP were then assessed at ages 10 and 15. Cumulative adverse events was associated with greater levels of inflammation in both childhood and adolescence (Slopen, Kubzansky, McLaughlin, & Koenen, 2013). In other studies, African Americans and older adults reporting childhood adversity showed greater levels of circulating IL-6 and TNF- $\alpha$  (Kiecolt-Glaser et al., 2011; Slopen et al., 2010).

One limitation in this area of research is the focus on adults. Examination of the early adversity-inflammation link during earlier life stages is important given that many chronic conditions related to inflammation are understood to be life course diseases that begin to develop relatively early in life. For instance, preclinical signs of cardiovascular disease, such as metabolic risk and signs of atherosclerosis, can be detected in adolescence (Cook, Weitzman, Auinger, Nguyen, & Dietz, 2003; Strong et al., 1999). Shifting the focus to younger samples can help us better understand when this link emerges and when might be a crucial time to intervene.

When studying the link between early adversity and inflammation during earlier life stages, it may be important to go beyond baseline measures of inflammation. Given that low-grade chronic inflammation develops over time, differences in systemic levels of inflammatory markers at baseline may not emerge until later in life (Slopen, Koenen, & Kubzansky, 2012). To the extent that early adversity programs immune cells to have a pro-inflammatory tendency when challenged (Miller et al., 2011), the effects of early adversity on inflammation may be better observed in the context of biological or psychosocial threat. Consistent with this idea, past studies have found that while chronic interpersonal stress during adolescence and harsh family climate in early life were not related to baseline circulating levels of inflammatory markers, they were associated with exaggerated inflammatory production in response to microbial threat among female adolescents (Miller & Chen, 2010; Miller, Rohleder, & Cole, 2009). Similarly, in a study of adolescent males and females, family chaos was related to greater stimulated proinflammatory cytokine production, but not to circulating levels of baseline inflammation (Schreier, Roy, Frimer, & Chen, 2014).

Although there has been some work examining how adversity relates to inflammatory responses to biological threat, examination of how early adversity relates to inflammation in

response to psychosocial threat has been scarce. Most studies have focused on baseline levels of inflammation, and only two studies to my knowledge have examined how early family stress affects inflammatory responses to stress. One study found that adults who experienced childhood maltreatment mounted a greater IL-6 response to a laboratory social stressor (Carpenter et al., 2010). The other study found that only depressed patients with a history of maltreatment exhibited greater inflammatory responses to stress (Pace et al., 2006). The lack of examination of how early adversity affects inflammatory reactivity to stress is particularly surprising given that heightened inflammatory responses to stress over time is believed to contribute to chronic inflammation and have consequences for health. In support of this notion, greater IL-6 and fibrinogen responses to stress have been shown to predict greater increases in ambulatory blood pressure over three years independent of initial ambulatory blood pressure and levels of IL-6, age, gender, smoking, body mass index (BMI), and blood pressure responses to stress (Brydon & Steptoe, 2005). Although there is substantial evidence purporting a link between early family stress and inflammation, more work is needed to determine the effects of early family stress on inflammatory reactivity to psychosocial stress and on inflammatory processes during childhood and adolescence.

Another gap in the literature on inflammatory effects of early adversity is that underlying mechanisms are not completely understood. Theoretical models, including the Risky Families Model (Repetti et al., 2002) and the Biological Embedding Model (Miller et al., 2011), suggest a number of primary biological and psychosocial pathways that link early adversity to heightened inflammation and ultimately to poor physical health outcomes. Putative pathways include disruptions in functioning of hypothalamic-pituitary-adrenal (HPA)-axis and the sympathetic nervous system (SNS), as well as in, cognitive appraisals, emotion processing, and social

relationships. Empirical work showing links between early family stress and sleep and between sleep and inflammation suggest that disruption in sleep may also mediate the link between early family stress and heightened inflammation. Despite theoretical and empirical work suggesting multiple pathways of different systems, very little work has tested these pathways in a single study. In general, research on the effects of early adversity on different systems has remained disparate. Thus, more studies are needed to test theoretical models and enhance our understanding of underlying mechanisms.

### **Biobehavioral Pathways: HPA Axis, SNS, and Sleep**

Prior research suggests that early family stress can alter the functioning of the HPA-axis and SNS and disrupt sleep processes. These biological processes are known to play a crucial role in regulating inflammatory processes. Thus, disruptions in HPA and SNS functioning and sleep may mediate the link between early adversity and increased inflammation.

***HPA function.*** The HPA axis is one of the two major biological stress systems that facilitate responses to threat. When stress is perceived, the paraventricular nucleus in the hypothalamus secretes corticotrophin releasing hormone (CRH). CRH stimulates the anterior pituitary to secrete adrenocorticotrophic hormone, which then stimulates the adrenal cortex to produce and release cortisol. In a negative feedback loop, cortisol binds to glucocorticoid receptors in several brain regions, including the hippocampus, PFC, amygdala, and hypothalamus, suppressing CRH production and the HPA stress response.

A number of various cell types express glucocorticoid receptors, including immune cells. When bound to glucocorticoid receptors on immune cells, a number of intracellular interactions occur that inhibit activity of NF- $\kappa$ B, a transcription factor that plays a key role in the expression of inflammatory genes. Cortisol, then, is anti-inflammatory and protects against negative effects

of an exaggerated or sustained inflammatory response (Glezer & Rivest, 2004; Irwin & Cole, 2011; Rohleder, 2011). Indeed, low levels of cortisol have been related to higher systemic levels of inflammatory markers (Kunz-Ebrecht, Mohamed-Ali, Feldman, Kirschbaum, & Steptoe, 2003; Rohleder, 2014).

A large literature has documented a link between early adversity and HPA axis functioning, although a complicated picture has emerged, with studies linking early life stress to both hyper- and hypo-cortisolism. For instance, family conflict, harsh discipline, parental loss, maltreatment, and maternal stress and depression [which increase behaviors of neglect, psychological aggression, and physical assault (Lovejoy, Graczyk, O'Hare, & Neuman, 2000; Turney, 2011)], are associated with higher levels of cortisol in children both at baseline (Ashman, Dawson, Panagiotides, Yamada, & Wilkinson, 2002; Essex, Klein, Cho, & Kalin, 2002) and in response to an acute stressor (Bugental, Martorell, & Barraza, 2003; Fries, Shirtcliff, & Pollak, 2008; Luecken & Appelhans, 2006; Sullivan, Bennet, & Lewis, 2013). Higher levels of cortisol related to early life stress have also been observed in adults. More specifically, maternal separation, poor parenting, and maltreatment have been related to greater cortisol reactivity to stress and greater basal levels of cortisol (e.g., Engert, Buss, et al., 2010; Heim et al., 2002; Kumari, Head, Bartley, Stansfeld, & Kivimaki, 2012).

Paradoxically, early adversity has also been related to a downregulation of the HPA axis. Children in the foster care system have been shown to exhibit blunted morning cortisol production (Bruce, Fisher, Pears, & Levine, 2009), and children with clinically depressed mothers, parental loss, or a history of caregiver maltreatment have been shown to have lower levels of cortisol both at baseline and in response to an acute stressor (Dietz et al., 2013; Fernald, Burke, & Gunnar, 2008; Ouellet-Morin et al., 2011). This blunted pattern of cortisol secretion in

response to acute stress is also evident among adolescents and adults who have experienced early life stress, including maltreatment, poor parental care, parental loss, and an overall risky family environment (e.g., Armbruster et al., 2011; Carpenter et al., 2007; Carpenter, Shattuck, Tyrka, Geraciotti, & Price, 2011; Carpenter et al., 2009; Engert, Efanov, et al., 2010; Luecken, Kraft, & Hagan, 2009; MacMillan et al., 2009; Taylor, Karlamangla, Friedman, & Seeman, 2011).

Although research has yet to determine why and how early adversity leads to different effects on the HPA axis, both hyper- and hypo-cortisolism are thought to represent dysregulation of the HPA axis (McEwen, 1998) with implications for inflammatory processes. Chronically high levels of cortisol secretion are thought to contribute to glucocorticoid receptor insensitivity, making it more difficult for immune cells to “hear” cortisol’s anti-inflammatory signals (Cohen et al., 2012; Miller, Cohen, & Ritchey, 2002). Thus, high levels of cortisol can eventually lead to elevated levels of inflammation. In the case of hypocortisolism, there simply may be insufficient amounts of cortisol to effectively downregulate and terminate inflammation. Despite known connections between the HPA axis and inflammatory processes, studies on the biological effects of early adversity have not examined how early adversity-related alterations in cortisol output affect inflammatory processes. Therefore, one of the primary aims of the current study is to examine how early family stress relates to HPA axis functioning and whether cortisol output – either elevated or reduced – underlies the early adversity-inflammation link.

**SNS.** The SNS is the other biological stress system that facilitates responses to threat. Perception of threat stimulates the neurons in the hypothalamic paraventricular nucleus, which projects to sympathetic preganglionic cells in the thoracic spinal cord (Zagon & Smith, 1993). These cells synapse with cells of the adrenal medulla, which secretes the catecholamines, epinephrine and norepinephrine, into systemic circulation. Perception of stress also releases

norepinephrine into local microenvironments of vasculature, organs, and tissues via SNS neural fiber innervation (Irwin & Cole, 2011). Norepinephrine, in turn, activates adrenergic receptors to affect inflammatory processes. Norepinephrine can have both anti- or pro-inflammatory effect depending the adrenergic receptor subtype that it activates, specific tissue, and local concentration of norepinephrine (McNamee et al., 2010; J. H. Yang, Lee, Kim, Suh, & Chong, 2012). When bound to alpha 2 and beta adrenergic receptors, norepinephrine stimulates NF- $\kappa$ B (Bierhaus et al., 2003) and therefore can upregulate pro-inflammatory gene expression in monocytes (Cole et al., 2010; Grisanti et al., 2011; Irwin & Cole, 2011).

Relative to the number of studies examining the effects of early adversity on HPA axis function, few studies have examined the effects of early adversity on SNS functioning. Similar to HPA axis findings, these studies have yielded mixed results. For instance, studies of youth that utilize impedance cardiography to assess SNS activity have shown that children exposed to neglect, family stress (e.g., parental depression, anger, and role overload, and financial and parenting stress), and aggressive marital conflict exhibit greater sympathetic activity to laboratory challenges (El-Sheikh, 2005; Ellis, Essex, & Boyce, 2005; Oosterman, De Schipper, Fisher, Dozier, & Schuengel, 2010). Consistent with these findings, youth with major depression or post-traumatic stress disorder with histories of maltreatment have been shown to have higher levels of catecholamines (De Bellis, 2001). More recent studies have assessed SNS functioning via salivary alpha-amylase (sAA) and have shown differing results. In one study, poverty was associated with lower levels of sAA among one-year-old children in one study (Hill-Soderlund et al., 2015). In another study, intrusive parenting assessed at 2.5 years old is predictive of higher levels of sAA at 6 years old (Z. E. Taylor et al., 2013). A study of adolescent girls showed that

diurnal sAA levels did not differ between sexually abused adolescents with PTSD and healthy controls (Keeshin, Strawn, Out, Granger, & Putnam, 2015).

Studies of adults have primarily relied on measures of blood pressure and heart rate to index SNS activity. These studies show that as adults, individuals who experienced stress (i.e., abuse, neglect, high levels of family conflict, illness, loss) in early life exhibit increases in heart rate and blood pressure both at rest and in response to acute stress (Gatt et al., 2009; Heim et al., 2000; K. T. Larkin, Frazer, & Semenchuk, 1996; K. T. Larkin, Frazer, & Wheat, 2011; Luecken, 1998; Taylor, Lerner, Sage, Lehman, & Seeman, 2004). However, not all studies have found this relation, with some studies showing no relation with early adversity (K. T. Larkin et al., 2011; Luecken & Roubinov, 2012) and others showing that more early adversity is related to lower heart rate and blood pressure (Leitzke, Hilt, & Pollak, 2015; Lovallo, 2013).

Although there has been growing interest in how early adversity may affect SNS functioning at different stages in the lifespan, the literature remains sparse and has yielded mixed findings. Furthermore, studies have not examined how early adversity-related changes in SNS functioning may impact inflammation despite the fact that the SNS is known to modulate inflammatory processes. To address these gaps, a primary aim of the current study is to characterize how early adversity may shape SNS activity and how SNS activity, in turn, relates to inflammatory activity.

***Sleep.*** Although not a primary biological stress system, sleep is a biobehavioral process important for inflammation that can be affected by stress. An increasing number of studies support the regulatory role of sleep on inflammatory processes. For instance, young adults who were randomly assigned to receive 4.2 hours of sleep for ten consecutive nights exhibited a 5-fold increase in levels of CRP from baseline to the end of the experimental period whereas their

non-sleep deprived counterparts exhibited no change in levels of CRP (Meier-Ewert et al., 2004). In another sleep deprivation study, those who received 6 versus 8 hours of sleep for one week showed increases in levels of IL-6 whereas those who did not lose sleep showed no changes in levels of IL-6 (Vgontzas et al., 2004). Other studies restricting sleep for multiple consecutive nights have replicated these findings (Frey, Fleshner, & Wright Jr., 2007; Haack, Sanchez, & Mullington, 2007; Irwin et al., 2008; Shearer et al., 2001; van Leeuwen et al., 2009), suggesting that shorter sleep duration results in increased inflammation.

Although most studies have focused on the relation between sleep duration and inflammation, poorer sleep quality has also been shown to be associated with higher levels of inflammation. For instance, in observational studies using objective measures of sleep, including polysomnography, greater sleep latency (i.e., time it takes to fall asleep) and sleep efficiency were associated with higher levels of IL-6 the following morning (Friedman et al., 2005; Hong, Mills, Lored, Adler, & Dimsdale, 2005; Mills et al., 2007). Similarly, self-reported poorer sleep quality, more frequent trouble falling asleep, and greater sleep latency and sleep disturbance are associated with greater levels of systemic inflammation cross-sectionally and longitudinally (Cho, Seeman, Kiefe, Lauderdale, & Irwin, 2015; Ferrie et al., 2013; Suarez, 2008) and with stimulated production of inflammatory cytokines (Prather et al., 2009).

Notably, early adversity has been associated with sleep disruptions. A recent systematic review found that 28 out of 30 studies found statistically significant associations between more early family stress and a greater likelihood to develop clinical sleep disorders in adulthood (Kajeepeta, Gelaye, Jackson, & Williams, 2015). Studies have also found a similar association for subclinical sleep problems. For instance, maltreated children have been shown to have greater sleep latency and decreased sleep efficiency compared to their non-maltreated

counterparts (Glod, Teicher, Hartman, & Harakal, 1997). Other adverse experiences, such as marital conflict and community violence, have also been associated with shorter duration of sleep and decreased sleep percent in children and adolescents (Cooley-Quille & Lorion, 1999; El-Sheikh, Buckhalt, Mize, & Acebo, 2006). Disrupted sleep as a result of early adversity may persist into adulthood. Adults who report maltreatment or other adverse experiences during childhood (i.e., parental separation, chronic financial difficulties, familial conflict, illness or alcohol problems in family member) report poorer sleep quality, more trouble falling and staying asleep, feeling tired despite a good night's sleep, and greater use of sleep medication (Chapman et al., 2013; Chapman, Whaton, et al., 2011; Greenfield, Lee, Friedman, & Springer, 2011; Koskenvuo, Hublin, Partinen, Paunio, & Koskenvuo, 2010). Similarly, older adults with a history of childhood emotional abuse report having trouble falling asleep and falling asleep after waking up during the sleep period (Poon & Knight, 2011).

Taken together, these findings suggest that disrupted sleep may be a pathway by which early adversity increases inflammation. However, to our knowledge, no study to date has examined this pathway. As such, the proposed study examines how early adversity affects sleep and investigates whether potential sleep disruptions may mediate the link between early adversity and inflammation.

### **Psychosocial Pathways: Cognitive Appraisal, Emotion Reactivity, and Social Relationships**

The family environment plays a critical role in the development of cognitive appraisal, and emotion processes. Caregivers facilitate development of these psychosocial processes by scaffolding responses to arousing stimuli and events, sensitively responding, helping navigate social interactions, and modeling social interactions and emotional responses. Through these interactions with family members and their observations of familial relationships, children learn

how to behave socially, whether the environment is safe, and whether they can depend on their environment to provide emotional security (Luecken, Roubinov, & Tanaka, 2013; Repetti et al., 2002). These psychosocial processes, in turn, have been shown to modulate inflammatory processes. Consequently, a stressful family environment may increase inflammation by disrupting social, cognitive, and emotional development.

***Cognitive appraisal.*** The family context helps shape children's information processing, and a stressful home environment can lead to attentional biases towards threat. Increasing evidence supports this notion. For instance, several neuroimaging studies have demonstrated that childhood maltreatment is linked to greater amygdala reactivity to threatening interpersonal cues among youth (Bogdan, Williamson, & Hariri, 2012; McCrory et al., 2013; Tottenham et al., 2011). This has also been observed in adults (Dannlowski et al., 2012; Fonzo et al., 2016; Redlich et al., 2015; van Harmelen et al., 2012), suggesting that early adversity may have long-term effects on threat perceptions. Behavioral studies have shown that early family stress leads to heightened threat appraisals. For instance, children who perceive less warmth and acceptance from their parents have been shown to appraise their environment as more highly threatening (Davies & Cicchetti, 2004). Lower family SES has also been associated with appraising negative and ambiguous social situations as more threatening and involving more hostile intent and anger among adolescents (Chen et al., 2006; Chen, Langer, Raphaelson, & Matthews, 2004; Chen & Matthews, 2001). Similarly, among adults, growing up in a low family SES household was related to higher threat appraisals (Miller et al., 2011).

Theoretical work indicates that cognitive appraisals are critical to stress processes, as appraisals of stimuli and events determine whether an individual experiences stress and biological stress systems become activated (Lazarus, 1966; Lazarus & Folkman, 1984). Some

empirical work supports this notion. Observational studies have shown a positive association between perceptions of stress and heightened inflammation (Chen et al., 2006; McDade, Hawkey, & Cacioppo, 2006). Experimental studies have shown similar findings. One study found that higher threat appraisals were related to greater stimulated production of TNF- $\alpha$  and IL-6 in response to an acute stressor (Wirtz et al., 2007). Another study found that higher anticipatory threat appraisals of a stressor predicted lower potential for effective wound healing, as measured by macrophage microbicidal potential (Kuebler et al., 2015). Together, findings from these studies support the idea that greater threat appraisals may be a viable pathway linking early family stress to heightened inflammation.

***Emotion reactivity.*** How emotions are displayed and regulated in familial interactions contributes to emotion processing (Luecken et al., 2013; Repetti et al., 2002). Thus, a stressful family environment characterized by conflict, unresponsivity, or hostility can lead to difficulties in processing emotions, especially during emotionally arousing events. Individuals from such family environments are less accurate at identifying emotional expressions and responses; consequently, they experience negative emotions of greater intensity and tend to be more emotionally reactive (Miller et al., 2011; Repetti et al., 2002). For example, in a daily diary study of over 900 adults, low quality maternal relationships during childhood were associated with greater psychological distress in response to daily stressors (Mallers, Charles, Neupert, & Almeida, 2010). Other daily diary studies have also found that childhood trauma is related to greater increases in negative affect in response to daily stressors (Glaser, van Os, Portegijs, & Myin-Germeys, 2006; Infurna, Rivers, Reich, & Zautra, 2015). Similarly, a harsh family environment during childhood has been related to greater emotional reactivity to acute laboratory stressors (McLaughlin et al., 2010), and emotional abuse experienced in childhood has been

related to increased depressive symptoms in response to stressful life events (Shapero et al., 2014). In addition to exhibiting greater emotional reactivity to stress, individuals with experiencing early adversity find it more difficult to recover emotionally from stressful events (Shields & Cicchetti, 1998).

Heightened negative emotional responses to stress likely have implications for inflammatory processes. There is substantial evidence that baseline negative emotions are linked to higher levels of inflammatory markers (Howren, Lamkin, & Suls, 2009; Marsland, Prather, Petersen, Cohen, & Manuck, 2008; Miyamoto et al., in press; O'Donovan, Slavich, Epel, & Neylan, 2012), and a growing body of work specifically links greater negative emotional reactivity to greater inflammation. These studies provide converging initial evidence for a positive association between emotional reactivity and inflammation. In a daily diary study, heightened negative reactivity to stress on a day-to-day basis predicted higher levels of CRP among women (Sin, Sloan, McKinley, & Almeida, 2016). Likewise, several experimental studies have shown that greater anger and anxiety responses to an acute laboratory stressor are associated with greater IL-6 responses to the stressor (Carroll et al., 2011; Moons & Shields, 2015; Puterman et al., 2014). Other experimental studies have shown that fear responses to a social stressor and inductions of guilt and shame are related to greater increases in proinflammatory markers (Dickerson, Kemeny, Aziz, Kim, & Fahey, 2004; Moons, Eisenberger, & Taylor, 2010). Collectively, findings from the literature on early adversity and emotional development and from the psychoneuroimmunology literature suggest that to the extent that early adversity leads to greater emotional reactivity to stress and prolongs emotional recovery from stress, inflammatory responses to stress may be exaggerated among those with a history of early adversity.

***Social relationships.*** Parent-child interactions and observation of familial relationships guide development of social competence and relationship schema that underlie social functioning and the development of close relationships (Grusec, 2011). Thus, conflictual, unsupportive familial relationships can compromise the acquisition and development of social skills (Miller et al., 2011; Repetti et al., 2002). Supporting this notion, insensitive parenting during childhood was related to less social competence from first to sixth grade (Boyer & Nelson, 2015), and less family cohesion in adolescence predicted more aggressive behaviors 6 years later in young adulthood (Fosco, Caruthers, & Dishion, 2012). Physical abuse during childhood has also been shown to prospectively predict greater social withdrawal during adolescence (Lansford et al., 2002) and to more peer nominations of aggressive behavior (Teisl & Cicchetti, 2008). Similarly, greater family conflict has been related to antisocial behavior during adolescence (Klahr, Rueter, McGue, Iacono, & Burt, 2011), aggression (Fosco et al., 2012) and to decreased sensitivity and responsiveness to peers (Herrera & Dunn, 1997).

Maladaptive social behaviors can lead to difficulties in developing and maintaining social relationships of high quality. Consequently, individuals who grew up in a stressful family environment are more likely to have lower quality relationships. For example, parental divorce has been related to less intimate romantic relationships in young adulthood (Cui & Fincham, 2010) and less warm and caring relationships with parents during childhood was related to greater fear of intimacy (Phillips et al., 2013). Maladaptive parenting and maltreatment in childhood have also been shown to prospectively predict interpersonal difficulties, including difficulty making new friends, a lack of close friends, and/or having poor friendships (Johnson et al., 2002). A nationally representative study similarly found that childhood adversity was associated with greater strain in close relationships among adults, especially among Black men

(Umberson, Williams, Thomas, Liu, & Thomeer, 2014). Individuals who experienced family-related stress during early life are also liked less by others, feel lonely, and perceive less social support (Kamiya, Doyle, Henretta, & Timonen, 2014; Repetti et al., 2002) .

Social relationships in turn may have implications for inflammatory processes. Insufficient or poor relationships are considered to be a source of interpersonal stress, which can increase sensitivity to subsequent stress and result in exaggerated stress responsivity (Hawkley & Cacioppo, 2010). Furthermore, social support and quality social relationships are important coping resources known to attenuate physiological consequences of stress (Eisenberger, Taylor, Gable, Hilmert, & Lieberman, 2007; S. E. Taylor, Welch, Kim, & Sherman, 2007; Uchino, 2006). Individuals experiencing early family stress, then, may be exposed to more interpersonal stress and be more sensitive to stress while not having adequate social support that can protect against the effects of stress. This may translate to exaggerated reactivity of inflammation as well as of the biological stress systems.

Relatively few studies have examined the link between characteristics of social relationships and inflammatory reactivity. However, these studies show that a lack of or poor social relationships is related to exaggerated inflammatory responses to stress. One study showed that more negative social interactions in daily life were related to enhanced inflammatory responses to a subsequent social stressor (Chiang, Eisenberger, Seeman, & Taylor, 2012). Another study showed that adults reporting less social connection exhibited higher stimulated production of inflammation after an acute stress compared to those reporting higher levels of social connection (Jaremka et al., 2013). Consistently, another experimental study showed that presence of an unsupportive or neutral figure led to greater increases in inflammatory reactivity to stress relative to the presence of a supportive figure, especially among individuals who

perceived to have low childhood SES (John-Henderson, Stellar, Mendoza-Denton, & Francis, 2015). In the context of marriage, experimental studies show that hostile behavior during marital conflict and avoidance of intimacy and dependency augment inflammatory responses to the marital conflict (J. P. Gouin et al., 2009; Kiecolt-Glaser et al., 2005)

More studies have examined basal levels of inflammation, although findings have not been entirely consistent. For instance, in MIDUS, social support in close relationships predicted lower levels of inflammation whereas social strain predicted higher levels of inflammation (Y. C. Yang, Schorpp, & Harris, 2014). Similarly, in NHANES, decreased social integration was related to higher levels of inflammation (Y. C. Yang, McClintock, Kozloski, & Li, 2013). By contrast, a positive association between social support and inflammation has been observed (Glei, Goldman, Ryff, Lin, & Weinstein, 2012), and several studies have found no relation between social integration and social support and inflammation (Bajaj et al., in press; McDade et al., 2006; Uchino et al., 2016).

There is consistent evidence for the link between early family stress and poor social relationships. The link between social relationships and inflammation is less clear, though there is some evidence suggesting a link. Taken together, studies from these different literatures begin to support theoretical models positing that impaired social relationship due to early adversity may contribute to the heightened inflammation. Given that the effects of early adversity on social functioning and on physiological processes have been examined in separate studies, more studies empirically evaluating whether deficits in social processes underlie the early adversity-health link are needed.

### **Current Study**

Prior work has documented a relation between greater early family stress and higher levels of inflammation. Collectively, findings from various literatures and theoretical models suggest a number of viable biobehavioral and psychosocial pathways linking early family stress to heightened inflammation. However, key questions remain unanswered, including whether early family stress impacts inflammatory reactivity to stress and whether disruptions in biobehavioral and psychosocial processes account for the effects of early family stress on inflammatory processes. Thus, the overall goal of the present study was to examine the relation between early family stress and inflammatory reactivity to an acute social stress and to probe the underlying biobehavioral and psychosocial pathways in a sample of late adolescents.

**Primary aims.** The present study had three primary aims. **Aim 1** was to examine the association between early family stress and inflammation at baseline and in response to an acute social stressor. We hypothesized that early family stress be associated with greater levels of baseline inflammation and inflammatory reactivity.

**Aim 2** was to examine whether disruptions in HPA axis and SNS functioning and sleep mediate the association between early family stress and inflammatory activity. To this end, we probed the relations between early family stress and HPA axis and SNS functioning and sleep as well as the relations between these biobehavioral processes and inflammatory activity. We hypothesized that early family stress would be associated with alterations in cortisol reactivity or prolonged recovery, enhanced sAA reactivity or delayed recovery, and poorer sleep. We also hypothesized that these, in turn, would be associated with heightened inflammatory reactivity.

**Aim 3** was to determine whether disruptions in cognitive appraisals, emotional reactivity, and social relationships mediate the association between early family stress and inflammatory activity. To this end, we examined the links between early family stress and cognitive appraisals,

emotional reactivity, and social relationships. Additionally, we examined the links between these psychosocial factors and inflammatory reactivity. We hypothesized that early family stress would be related to higher threat appraisals, greater negative emotional reactivity, and poorer social relationships. We also hypothesized that these, in turn, would contribute to heightened inflammatory reactivity.

**Secondary aims.** We also examined the associations between psychosocial functioning (cognitive appraisals, emotional reactivity, social relationships) and HPA axis and SNS functioning given prior work showing that these psychosocial processes modulate HPA axis and SNS functioning. For example, higher anticipatory threat appraisals of an upcoming stressor have been related to exaggerated cortisol reactivity (Gaab, Rohleder, Nater, & Ehlert, 2005; Schlotz, Hammerfald, Ehlert, & Gaab, 2011) and greater cardiovascular reactivity (Chen & Matthews, 2001; Maier, Waldstein, & Synowski, 2003). Likewise, greater negative emotional responses to an acute social stressor have been linked to greater HPA and cardiovascular responses (Davies, Sturge-Apple, Cicchetti, Manning, & Zale, 2009; Luecken, Appelhans, Kraft, & Brown, 2006). A large literature has also demonstrated a link between lower levels of social support, higher levels of loneliness, and poorer overall quality of close relationships, and altered HPA axis functioning (e.g. flatter diurnal slope, blunted cortisol awakening response; exaggerated responses to acute stress) (Burton, Bonanno, & Hatzenbuehler, 2014; Drake, Sladek, & Doane, 2016; Eisenberger et al., 2007; Ho, Fong, Chan, & Chan, 2013; Hostinar, Sullivan, & Gunnar, 2014; Sladek & Doane, 2015), as well as to cardiovascular responses to stress (Gramer & Supp, 2014; Nausheen, Gidron, Gregg, Tissarchondou, & Peveler, 2007; Ong, Rothstein, & Uchino, 2012; Uno, Uchino, & Smith, 2002). In light of these findings,

we hypothesized that higher threat appraisals, greater emotional reactivity, and poorer social relationships would be related to alterations in HPA axis and SNS functioning.

**Exploratory aims.** We had two exploratory aims. First, we tested whether effects of early family stress on inflammatory, biobehavioral, and psychosocial processes were moderated by gender and ethnicity. There is some evidence to suggest differential effects of early adversity by gender. For instance, in one study, women with a history of childhood maltreatment were tended to develop alcohol dependence more quickly than men and non-maltreated women (Oberleitner, Smith, Weinberger, Mazure, & McKee, 2015). The association between early adversity and increases in BMI and cardiovascular disease has also been shown to be stronger in women compared to men (Bae, Wickrama, & O'Neal, 2014; Hosang et al., 2013). Studies have also shown that for male youth, maltreatment was most strongly related to poor behavioral outcomes and depressive symptoms earlier in adolescence, but this link diminished over time; by contrast, for female youth, the link between maltreatment and poor behavioral outcomes and depressive symptoms remained unchanged or increased over time (Godinet, Li, & Berg, 2014; St Clair et al., 2015). Other studies have found no gender differences in the effects of early adversity (Wickrama, Conger, Lorenz, & Jung, 2008; Wickrama, Conger, Wallace, & Elder Jr, 2003).

There is also some evidence that the effects of early adversity may vary by ethnicity. The link between early adversity and BMI was stronger among White compared to Asians (Bae et al., 2014). In MIDUS, early adversity was related to higher levels of inflammation among African-Americans, but not Whites (Slopen et al., 2010). Similarly, in the Americans' Changing Lives Study, another nationally representative study, early adversity was related to greater relationship strain among African Americans, but not Whites (Umberson et al., 2014). By contrast, another

study found no moderation of ethnicity in the link between early adversity and behavioral problems (Godinet et al., 2014). Based on these studies, we tentatively hypothesized that some of the effects of early family stress would be more profound for females than for males. Given the past findings on ethnic differences of the effects of early adversity, we also hypothesized that some of the effects of early family stress would vary by ethnicity. However, we did not have explicit hypotheses given mixed findings on ethnic differences and the fact that the current samples consisted of individuals from Latino and European backgrounds, but few studies have compared these ethnic groups.

Second, we explored whether specific types of early family stressors are differentially related to inflammatory, biobehavioral, and psychosocial functioning. Theoretical work suggests that different types of family stressors may have differential and even unique effects on biological and psychosocial development. For instance, it has been proposed that threatening family environments results in alterations in neural development underlying fear learning whereas deprivation impacts other aspects of neural development, namely proliferation and pruning of (McLaughlin, Sheridan, & Lambert, 2014). Emerging empirical work also points to the possibility that specific types of family stressors might have distinct effects on inflammatory and biological stress systems. For instance, one study found that only family chaos was associated with higher inflammation independent of abuse and neglect (Crosswell, Bower, & Ganz, 2014). Another study found that physical abuse was associated with quicker HPA reactivity to acute stress, emotional abuse was associated with delayed recovery to acute stress, and non-intentional trauma was related to high levels of cortisol at bedtime (Kuhlman, Geiss, Vargas, & Lopez-Duran, 2015). Based on these results, we hypothesized differential effects of

specific types of early family stressors. Following previous research (Crosswell et al., 2014), we focused specifically on the effects of abuse, neglect, and a chaotic home environment.

## **Methods**

### **Participants**

Participants were 91 late adolescents ( $M_{age} = 18.37$ ,  $SD = .51$ ; 57.14% females) from European (37.36%) and Latino (62.64%) backgrounds. Most of the Latino participants were from immigrant families, with 8.9% of Latino being first-generation (i.e., foreign-born), and with 58.9% of Latinos being second generation (i.e., US-born with at least one foreign-born parent). The majority (89.7%) of participants from European backgrounds were third generation or greater (i.e., adolescent and both parents US-born).

Participants were mostly from middle-class backgrounds: median household income reported by primary caregivers was \$79,000 (range = \$11,000 – \$350,000). Primary caregivers also indicated their own and their spouse's highest level of education completed, using an 11-point scale (*1 = some elementary school, 11 = graduated from medical, law, or graduate school*). Averaging education across parents revealed that on average, adolescents' parents completed some vocational or trade school ( $M = 7.44$ ,  $SD = 2.01$ ). Approximately 14.44% of participants had parents with less than a high school diploma, 7.78% had at least one parent with a high school diploma, 38.89% had at least one parent who completed vocational trade school or some college, 23.33% had at least one parent with a college degree, and 15.57% had at least one parent who completed at least some medical, law, or graduate school.

Participants were recruited from Wave 2 of the UCLA Family Health Study, a three-wave longitudinal study of parent-child dyads aimed to assess the role of psychosocial factors, including daily socio-emotional experiences, in the development of early risk for poor adult

health. The larger study consists of a home visit, a daily diary portion, and collection of biological markers at each wave. Recruitment for Wave 2 of the larger study began October 2013. We invited all Latino and European-American participants who were free of medical and psychiatric conditions, and were at least 18 years old to participate in the present study.

## **Procedure**

Participants first completed the larger study. Upon completion, they were pre-screened to ensure that they identified as Latino or European-American (other ethnicities were excluded due to insufficient numbers in the larger study) and did not have any chronic medical condition. Pre-screening was based on responses to questionnaires assessing medical history and ethnic identity that were collected as part of the larger Family Health Study. Participants who qualified were contacted via telephone and invited to participate in the present study.

During recruitment calls, participants were informed that the study entailed completing 5-minute sleep diaries for three consecutive mornings and a laboratory visit that would take approximately 2.5-3 hours. They were informed that the laboratory visit would involve performing cognitive challenges, completing questionnaires, and providing saliva samples and blood samples drawn multiple times via an indwelling intravenous (IV) catheter. They were also informed that the compensation was \$150. Female participants were also screened for current pregnancy and breast-feeding within the last six months.

Eligible participants who expressed interest in participating in the study were then scheduled for a laboratory visit at the Clinical and Translational Research Center (CTRC). Given the diurnal rhythm of cortisol and that many of the participants were still in high school, study sessions were scheduled to start anytime between the hours of 12pm and 3pm. Because particular health behaviors can influence functioning of the biological systems of interest, participants were

specifically instructed to refrain from consuming dairy products three hours before the session and to refrain from eating or drinking anything except water the hour prior to the visit.

Confirmation and reminder emails and texts with all the information reviewed during the recruitment calls were sent to participants.

Sleep diaries were mailed to participants approximately one week before their scheduled laboratory visit. Participants were instructed to complete these sleep diaries each morning for three consecutive mornings, including two mornings before the scheduled laboratory visit and the morning of the laboratory visit. This procedure for assessing perceived sleep was similar to that implemented in the larger Family Health Study. Participants confirmed that they received the sleep diaries in the mail via text messaging or email, whichever the participant preferred. The night prior to the start of the sleep diaries, participants were also reminded to start completing their sleep diaries the following morning.

On the day of the laboratory visit, a research assistant greeted participants at the Jules Stein parking lot and walked them to the CTRC. Upon arrival at the CTRC, the research assistant collected sleep diaries and obtained consent. A seasoned nurse then assessed vital signs and height and weight and proceeded to insert an indwelling intravenous catheter in the antecubital vein of the nondominant arm, a procedure routinely performed in hospitals and during medical examinations. Participants then watched a neutral-content video quietly for 20 minutes to facilitate acclimation to the testing environment and indwelling catheter. After this period, the first saliva and blood samples were collected and participants completed an emotion questionnaire to assess baseline emotions.

Next, participants were given instructions for the Trier Social Stress Task (TSST), a well-established laboratory stressor (Kirschbaum, Pirke, & Hellhammer, 1993) that reliably increases

inflammation (Steptoe, Hamer, & Chida, 2007). Participants were specifically instructed to prepare and deliver a speech on why they were the best candidates for their ideal jobs in front of an evaluative panel of expert interviewers. They were also informed that they would be given a second task that was to be explained by the judging panel. Participants were informed that they were going to be evaluated on the basis of their qualifications and their ability to communicate clearly and persuasively, and that their performance on the tasks was going to be compared to their peers who had already completed the tasks. After receiving instructions, participants completed measures of appraisals of the upcoming task. They then had five minutes to prepare for the upcoming task.

After the preparation period, participants delivered their speech in front of the evaluative panel consisting of research assistants trained to provide nonverbal negative feedback. Immediately afterwards, participants performed a five-minute mental arithmetic task that involved subtracting by 13's from 2,935 as quickly and accurately as possible. During this task, participants were urged to go more quickly if they got three consecutive answers correct and were instructed to start from the beginning each time they made a mistake.

Upon completing the TSST, participants provided a second saliva sample and completed questionnaires of their current emotions and appraisals of the tasks that they just completed. They then proceeded to complete other questionnaires. As they completed the questionnaires, additional saliva and blood samples were collected. After the final blood draw, the experimenter debriefed participants, emphasizing that the TSST was used to evoke an acute stress response, the panel was trained to look stoic, and that evaluations were not truly made. Lastly, participants were compensated \$150 before dismissed. Figure 1 shows a timeline of the experimental session.

## **Measures**

**Early family stress.** The primary measure of early family stress was the Risky Families (RF) questionnaire (S. E. Taylor, Lerner, et al., 2004). This measure assessed overall family environment during the first 15 years of life. On a scale from *1=not at all* to *5=very often*, participants indicated how often conflict, violence, harsh discipline, affectionate behaviors, neglect, and chaos/disorganization occurred. The RF questionnaire has been shown to have high agreement with clinical interviews assessing early life stress (S. E. Taylor, Lerner, et al., 2004). Cronbach's  $\alpha$  was .84 for the current sample, indicating good reliability.

To examine the unique and differential effects of particular types of family stressors, three subscales were created, including abuse, neglect, and chaotic home environment. The abuse subscale tapped into both physical and emotional abuse with two items assessing how frequently a parent pushed, grabbed, shoved, or slapped the participant and how frequently a parent swore at, insulted, put down, or threatened the participant. These two items were significantly correlated ( $r = .47$ ).

The neglect subscale consisted of three items that tapped into how attentive and affectionate adults in the home were towards the respondent. These items assessed how often a parent or other adult made the individual feel loved or cared for (reverse coded), showed physical affection (reverse coded), and left the individual to fend for him- or her-self. These items showed good internal consistency ( $\alpha = .81$ ).

The chaos subscale consisted of four items that tapped into how chaotic and conflict-ridden the home environment was. These items assessed the frequency of arguing or shouting between parents, presence of an alcoholic or drug user in the home, violence between adults, and perceived chaos or disorganization in the home. Cronbach's  $\alpha$  for these items was .64.

**Social relationships.** The 24-item Social Provisions Scale (SPS) (Cutrona & Russell, 1987) was used to assess multiple aspects of social relationships. The SPS is composed of six 4-item subscales that fall into broader categories of assistance-related and non-assistance related aspects of social relationships. Assistance-related social functions include (1) advice or information (i.e., guidance/informational support) and the (2) assurance that others can be depended on for tangible assistance (i.e., reliable alliance/tangible support). Example items include: “There is someone I could talk to about important decisions in my life” and “There are people I can depend on to help me if I really need it”. Non-assistance social functions include (3) others’ recognition of one’s competence and value (i.e., reassurance of worth), (4) provision of support or assistance to others (i.e., opportunity for nurturance), (5) a sense of belonging to a group (i.e., social integration), and (6) emotional closeness that provides a sense of security (i.e., attachment/emotional closeness). Example items of these dimensions include: “I have relationships where my competence and skill are recognized”, “There are people who depend on me for help”, “I feel part of a group of people who share my attitudes and beliefs”, and “I feel a strong emotional bond with at least one other person”. Participants indicated the degree to which they agreed with each item on a scale from 1=*strongly disagree* to 4=*strongly agree*. The SPS provides a score for each of the six subscales as well as an overall summary score (i.e., average score across subscales).

**Emotion processing.** Emotional reactivity to the TSST was assessed using items from the Positive and Negative Affect Schedule-Expanded Form (Watson & Clark, 1994). Items were drawn from scales assessing overall negative affect and specific dimensions of negative affect, including fear, hostility, guilt, and sadness. The negative subscale included the following 8 items: afraid, nervous, scared, hostile, guilty, shamed, upset, and distressed. Items from the fear

subscale included afraid, scared, frightened, nervous, and shaky. Items from the hostility subscale included angry and hostile. Items from the guilty subscale included guilty, ashamed, blameworthy, disgusted with self, and dissatisfied with self. Lastly, items from the sad subscale included sad, blue, and lonely. Using a scale ranging from 0=*not at all* to 4=*extremely*, participants reported on their current emotions immediately after watching the neutral content video (baseline) and after the TSST. The difference scores between these two time points were computed to index emotional reactivity to the TSST.

**Threat appraisal.** Threat appraisals were assessed using a questionnaire developed in previous research (Mendes, Blascovich, Major, & Seery, 2001). Appraisals were assessed immediately after the TSST instructions (anticipatory) and after completion of the TSST (retrospective). Participants responded to 11 items assessing perceived demands and resources to cope on a scale ranging from 1=*strongly disagree* to 7=*strongly agree*. Six items assessed perceived demands, including “this task is demanding,” “...is stressful,” “...is distressing,” “...is threatening”; “I am uncertain how I will perform”, and “this task requires a lot of effort”. Reliability was acceptable (anticipatory  $\alpha = .80$ ; retrospective  $\alpha = .72$ ). Resources to cope were assessed with 5 items, including “I have the abilities to perform well,” “I have the expectations to perform well,” “performing well is important to me,” “this task is a positive challenge,” and “I am the type of person who does well on these tasks.” There was good reliability (anticipatory  $\alpha = .84$ ; retrospective  $\alpha = .85$ ). The ratio to demands and resources was computed to index threat perceptions.

**Inflammation.** Pro-inflammatory cytokine interleukin (IL)-6 was assessed from plasma. IL-6 was chosen because it is sensitive to acute stress (Steptoe et al., 2007) and has been related to early family stress (Carpenter et al., 2010; Slopen et al., 2013). Six mL of blood was collected

immediately following the neutral content video, and 30, 60, and 90 minutes after TSST onset. These sampling times enable examination of inflammation at baseline and in response to the TSST (Steptoe et al., 2007).

Blood samples were collected into EDTA lavender-top tubes and placed on ice immediately after collection. They were then transported to the CTRL where they were centrifuged for acquisition of plasma, separated into three 1ml plasma aliquots, and stored at -80°C. Once all data were collected, these samples were transported to the UCLA Inflammatory Biology Core Laboratory where they were assayed for IL-6, using the Quantikine high sensitivity human IL-6 ELISA kits (R&D Systems, Inc., Minneapolis, MN). Samples were assayed in duplicate and each subject's samples were assayed in the same run. Intra- and inter-assay coefficients of variability were below 7%. The lower limit detection of the assay was .2 pg/mL; no samples were below this limit. Change scores were calculated from baseline to peak IL-6 (i.e., 90 minutes post-stressor) to index absolute magnitude of IL-6 increases in response to the TSST.

**HPA axis function.** Six saliva samples were collected throughout the experimental session: immediately after the neutral-content video (baseline), after the TSST, and 30, 45, 60, and 75 minutes after TSST onset. These sampling times allowed examination of HPA reactivity to and recovery from stress (Dickerson & Kemeny, 2004). Saliva samples were collected using oral swabs (Salimetrics). Participants placed the swab in their mouths for two minutes, allowing saliva to saturate the swab. Participants were instructed not to chew on the swab. Samples were placed on ice immediately following collection. At the end of the laboratory visit, they were then transported to the CTRL where they were stored at -80°C until shipped on ice to Dr. Clemens Kirschbaum, Director of the Laboratory of Biological Psychology at the Technical University of Dresden, Germany. Saliva samples were assayed for cortisol in duplicate using

chemiluminescence-immunoassays with high sensitivity (IBL, International, Hamburg, Germany). The intra- and inter-assay coefficients of variations were below 10%.

Cortisol values were log-transformed to correct for non-normality. Following previous research, area under the curve with respect to ground (AUC<sub>G</sub>) and increase (AUC<sub>I</sub>) were computed using an established trapezoid formula (Pruessner, Kirschbaum, Meinlschmid, & Hellhammer, 2003). Because AUC parameters do not distinguish between reactivity and recovery, change scores were also computed. Specifically, change scores between baseline and the peak sample (i.e., 30 minutes post-stressor) were computed to index cortisol reactivity. Change scores between peak sample and the last recovery sample (i.e., 75 minutes post-stressor) were computed to index cortisol recovery.

**Sympathetic activity.** The six saliva samples were also assayed for alpha-amylase, an enzyme secreted by salivary glands, which are under sympathetic control. Salivary alpha-amylase has been shown to predict norepinephrine (catecholamine secreted by the SNS) responses to stress, indicating that it reflects SNS activity (Thoma, Kirschbaum, Wolf, & Rohleder, 2012). Sampling times enabled examination of SNS reactivity to and recovery from the TSST (Nater et al., 2006; Nater et al., 2005). Samples were assayed in duplicate using an enzyme kinetic method. The intra- and inter-assay coefficients of variations were below 10 %.

To correct for non-normality, sAA values were log-transformed. Log-transformed values were then used to compute AUC<sub>G</sub> and AUC<sub>I</sub>. Change scores between baseline and the peak sample (i.e., immediately post-stressor) were computed to index sAA reactivity. Change scores between peak sample and the last recovery sample (i.e., 75 minutes post-stressor) were computed to index sAA recovery.

**Sleep.** Sleep was assessed via daily morning reports of the prior night's sleep and the Pittsburgh Sleep Quality Index (PSQI) (Buysse, Reynolds III, Monk, Berman, & Kupfer, 1989). For three consecutive mornings prior to the laboratory visit, participants indicated the time they turned off the lights to sleep last night, the number of minutes it took to fall asleep after turning off the lights, the number of times they awoke, the time they awoke in the morning, the time they got out of bed, and the difficulty they had getting out of bed. Items were taken from the Pittsburgh Sleep Diary and have been shown to correlate with actigraphy measures (Lockley, Skene, & Arendt, 1999). From these items we computed sleep duration, sleep latency, and sleep efficiency. Sleep duration for each night was the total number minutes of sleep during the in-bed period. Sleep latency was the reported number of minutes it took to fall asleep, and sleep efficiency was calculated as the percentage of actual sleep during the total time in bed. These sleep indices were averaged across the three nights.

During the laboratory visit, participants also completed the 19-item PSQI, a validated measure of sleep widely used in previous research. The PSQI assesses perceptions of sleep quality and disruptions over the past month. Traditional scoring was used to compute a global sleep quality score based on six sleep components (i.e., subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, and daytime dysfunction). Scores for each sleep component ranged from 0-3 and scores for total sleep range from 0 to 18, with higher scores indicating poorer sleep.

**Potential confounds.** Age, gender, ethnicity, BMI, SES, and depressive symptoms were also assessed, as they have been related to the study variables of interest (Champaneri et al., 2013; Charbonneau, Mezulis, & Hyde, 2009; Chen et al., 2004; Cohen, Janicki - Deverts, Chen, & Matthews, 2010; Dowd, Simanek, & Aiello, 2009; Goel, Kim, & Lao, 2005; Mezick et al.,

2008; O'Connor et al., 2009; Stetler & Miller, 2011; S. E. Taylor, Sherman, et al., 2004; Thase, 2006; Uhart, Chong, Oswald, Lin, & Wand, 2006). Participants reported on their date of birth, gender, ethnicity, and depressive symptoms using the Center for Epidemiologic Studies Depression Scale (Radloff, 1977). Nurses assessed participants' height and weight for BMI calculations, and participants' parents reported on their and their spouses' highest level of education as an index of SES in the larger study.

### **Statistical Analysis**

All statistical analyses were conducted using Stata 12.0 (StataCorp LP, USA). Descriptive statistics of all variables of interest were first examined. Additionally, histograms were plotted for the assessment of the distribution of each variable and any outliers. We also examined the bivariate correlations among study variables. We then examined whether the TSST elicited inflammatory, HPA, and SNS responses using a series of multilevel growth curve modeling. Lastly, hypotheses were tested using multilevel growth curve modeling and multiple regression analyses.

In general, multilevel growth curve modeling was used for analyses involving outcome variables with repeated measurements (i.e., IL-6, cortisol, sAA). The nesting of time points within individuals produces dependencies among observations within individuals and thus violates assumptions of independence of errors. Multilevel growth curve modeling accounts for the auto-correlation among repeated measurements within each individual. Furthermore, it allows for inclusion of all available data. As such, this approach is optimal for modeling change over time.

A series of two-level growth curve models were tested in which Level 1 modeled individual changes in IL-6, cortisol, or sAA as a function of time, and Level 2 modeled between-

person differences based on individual difference variables. Whether levels of IL-6, cortisol, or sAA varied as a function of experiences of early family stress or psychosocial factors was examined by grand-mean centering the variable of interest and adding it as a predictor of the intercept and slope at Level 2. In models examining whether IL-6 levels varied as a function of HPA and SNS responses, AUC and change scores of cortisol and sAA were entered at Level 2. Significant cross-level interactions between time and the variable of interest indicated moderation of the variable of interest on the association between time and the outcome variable. Potential confounding variables were controlled for by entering them as between-person predictors of the intercept at Level 2. Significant cross-level interactions were followed up with tests of simple slopes using mean splits given that for some variables there were only a few or no individuals either above or below one standard deviation.

Following past research (Carpenter et al., 2007; Carpenter et al., 2010; Carroll et al., 2011; Kirschbaum, Klauer, Filipp, & Hellhammer, 1995; Maruyama et al., 2012; Strahler, Mueller, Rosenloecher, Kirschbaum, & Rohleder, 2010), we also used multiple regression to conduct AUC and change score analyses of IL-6, cortisol, and sAA. In these sets of analyses, we used IL-6, cortisol, or sAA change scores indexing reactivity or recovery or AUC computations as outcome or predictor variables. For instance, in a model examining the relation between early family stress and inflammation, the difference score between baseline and peak IL-6 was regressed on RF scores. Likewise, in separate model examining the link between HPA axis functioning and inflammatory activity, cortisol AUCg, AUCi, and reactivity and recovery change scores were regressed on IL-6 change scores.

Multiple regression was also used for all other analyses not involving repeatedly assessed IL-6, cortisol, and sAA. This set of analyses consisted of examining the link between early

family stress and sleep and psychosocial variables.

All analyses controlled for sociodemographic characteristics, including age, gender, ethnicity, and SES, as these factors have been shown to be related to inflammation (O'Connor et al., 2009), HPA axis and SNS functioning (Dowd et al., 2009; El-Sheikh, Erath, Buckhalt, Granger, & Mize, 2008; Granger et al., 2007; Hinojosa - Laborde, Chapa, Lange, & Haywood, 1999; Hostinar & Gunnar, 2013; Stroud et al., 2009; Uhart et al., 2006), sleep (Dahl & Lewin, 2002; Goel et al., 2005; Mezick et al., 2008), and/or the psychosocial factors of interest (Charbonneau et al., 2009; Chen et al., 2004; Cohen et al., 2010; S. E. Taylor, Sherman, et al., 2004). Additionally, analyses with IL-6 as the outcome variable included BMI as a covariate given that prior research has demonstrated a robust link between inflammation and adiposity (O'Connor et al., 2009). We also tested the influence of BMI in models with HPA and SNS parameters as the outcome variables given adiposity has also been related to HPA axis and SNS functioning (Champaneri et al., 2013; Tataranni, Young, Bogardus, & Ravussin, 1997). Similarly, depressive symptoms were added as a covariate in follow-up analyses of all models given that depressive symptoms have been shown to related to all variables of interest (Hammen, 2005; Howren et al., 2009; Joormann & Vanderlind, 2014; Medina, Lechuga, Escandon, & Moctezuma, 2014; Stetler & Miller, 2011). Overall, results were not altered when adjusting for BMI or depressive symptoms. Consequently, results from more parsimonious models with these controls are reported. Results from models including BMI or depressive symptoms are reported only if they were found to either alter results or be significantly related to the outcome variable.

## **Results**

### **Descriptive Statistics**

Descriptive data of study variables are presented in Table 1. Participants were somewhat

overweight and CESD scores were relatively close to the cutoff score of 16, although there was considerable variability for both these variables. Overall, participants reported relatively low levels of early family stress. Approximately 60.44% of participants had an average RF score of 1 through 2, 31.07% had an average score of greater than 2 through 3, and 5.49% had an average RFQ score greater than 3. The average overall average RF score in the present sample is similar to that found in another study of adolescents that showed that RF scores were related to increasing stimulated production of IL-6 over time (Miller et al., 2010).

Bivariate correlations among study variables are presented in Tables 2a-2d. Higher RF scores were related to more depressive symptoms (Table 2a), lower cortisol AUCg (Table 2b), worse sleep (i.e., total PSQI sleep and PSQI day dysfunction; Table 2c), higher threat appraisals, and less supportive relationships (Table 2d). RF scores as well as putative psychosocial and biobehavioral mediators were not correlated with IL-6 reactivity.

### **Manipulation Check**

A series of unconditional growth models were tested to determine whether the TSST had the desired effect on inflammation, the HPA axis, and the SNS. We first focused on inflammatory responses with time and time<sup>2</sup> entered at Level 1. The specific model tested was:

$$(1) \text{ Level 1: } \ln IL6_{ij} = \beta_{0i} + \beta_{1i} \text{ time}_{ij} + \beta_{2i} \text{ time}_{ij}^2 + e_{ij}$$

$$\text{Level 2: } \beta_{0i} = \gamma_{00} + u_{0i}$$

$$\beta_{1i} = \gamma_{10} + u_{1i}$$

$$\beta_{2i} = \gamma_{20} + u_{2i}$$

Results from this model indicated that that the TSST elicited increases in IL-6. The linear term for time was non-significant ( $b(SE) = .002 (.03), p = .94$ ). However, the quadratic term for

time was significant ( $b(SE) = .04 (.01), p < .001$ ). As shown in Figure 2a, there was an accelerated increase from the 30-minute sample to the 90-minute sample.

Next, we examined whether the TSST was effective in activating the HPA axis by testing the unconditional growth model indicated in Equation 1, but with cortisol as the outcome variable. Sampling times were designed to capture both HPA reactivity to and recovery from the TSST. As such, the linear slope captures the cortisol increase in response to the TSST whereas the quadratic slope captures the deceleration in the curve. Results showed a significant effect of time ( $b(SE) = .27 (.03), p < .001$ ) and time<sup>2</sup> ( $b(SE) = -.06 (.01), p < .001$ ), indicating that the TSST elicited an HPA response. As expected, cortisol peaked 30 minutes post-TSST and returned to baseline by the 75 minutes post-TSST, as depicted in Figure 2b.

We then tested the unconditional growth model indicated in Equation 1, replacing IL6 with sAA as the outcome variable, to determine whether the stressor elicited an SNS response. Sampling times were designed to capture both SNS reactivity to and recovery from the TSST, and therefore the linear slope represents sAA increases in response to the TSST whereas the quadratic slope represents the deceleration in the curve. Results indicated that the TSST effectively activated the SNS with results showing a significant effect of time ( $b(SE) = .17 (.04), p < .001$ ) and time<sup>2</sup> ( $b(SE) = -.04 (.01), p < .001$ ). As shown in Figure 2c, sAA peaked immediately after the TSST.

### **Early Adversity and Inflammation (Primary Aim 1)**

Analyses next focused on testing hypotheses. First, we tested whether greater early family stress predicted heightened levels of IL-6. The specific model tested was:

$$(2) \text{ Level 1: } \ln \text{ IL6}_{ij} = \beta_{0i} + \beta_{1i} \text{ time}_{ij} + \beta_{2i} \text{ time}^2_{ij} + e_{ij}$$

$$\text{Level 2: } \beta_{0i} = \gamma_{00} + \gamma_{01} \text{ RF}_i + \gamma_{02} \text{ Age}_i + \gamma_{03} \text{ Gender}_i + \gamma_{04} \text{ Ethnicity}_i + \gamma_{05} \text{ SES}_i + \gamma_{06} \text{ BMI}_i$$

$$+ u_{0i}$$

$$\beta_{1i} = \gamma_{10} + \gamma_{11}RF_i + u_{1i}$$

$$\beta_{2i} = \gamma_{20} + \gamma_{21}RF_i + u_{2i}$$

As shown in Table 3, baseline levels of IL-6 varied by gender and BMI such that females and individuals with a higher BMI had significantly higher levels of IL-6 at baseline than males and those with lower BMI. There were no significant cross-level interactions between time and RF. As shown in Table 3 and Figure 3, early family stress was unrelated to IL-6 at baseline ( $p = .22$ ) and IL-6 reactivity ( $p = .54$ ). This suggests that early family stress did not moderate the association between time and IL-6.

As described above, we also conducted multiple regression analyses using change scores between baseline and peak IL-6 (i.e., 90 minutes post TSST) to index IL-6 reactivity. Results from these models similarly showed that RF scores were unrelated to baseline IL-6 ( $b(SE) = -.13 (.10), p = .19$ ) and changes in IL-6 ( $b(SE) = .04 (.06), p = .51$ ).

### **Early Family Stress, Biobehavioral Processes, and Inflammation (Primary Aim 2)**

Analyses next examined whether early family stress was related to biobehavioral processes (i.e., HPA and SNS function and sleep) and whether biobehavioral processes were in turn related to inflammation. We hypothesized that early family stress would be related to HPA, SNS, and sleep disruptions, and that disruptions in these systems would predict heightened inflammation.

**HPA axis.** A series of multi-level growth curve models and multiple regression models were tested to determine whether early family stress was associated with altered HPA activity and whether altered HPA activity was in turn associated with greater inflammation.

**Early family stress and HPA axis functioning.** We examined whether HPA responses varied by experiences of early family stress by testing a model similar to that indicated in Equation 2 except that cortisol was the outcome variable and BMI was not included as a covariate. As shown in Table 4, we found that RF scores were not associated with baseline levels of cortisol ( $p = .11$ ). However, there was a significant interaction between early family stress and time ( $p = .01$ ) and time<sup>2</sup> ( $p = .01$ ). Follow-up analyses testing the simple slopes for adolescents with high (above mean) and low (below mean) RF scores were conducted to interpret the cross-level interaction. As shown in Figure 4, individuals experiencing more early family stress tended to exhibit dampened cortisol reactivity to ( $b(SE) = .24 (.04), p < .001$ ) and recovery from ( $b(SE) = -.05 (.02), p < .001$ ) the TSST compared to individuals with lower RF scores [time:  $b(SE) = .29 (.04), p < .001$ ; time<sup>2</sup>:  $b(SE) = -.06 (.01), p < .001$ ].

Findings from regression analyses in which baseline cortisol and cortisol AUCg, AUCi, and reactivity and recovery changes scores were regressed on early family stress were consistent with those from multi-level growth curve modeling. There was no association between early family stress and baseline levels of cortisol ( $b(SE) = -.12 (.12), p = .31$ ). AUC analyses showed that early family was significantly related to lower cortisol AUCg ( $b(SE) = -21.98 (7.25), p = .003$ ). RF scores were not related to cortisol AUCi ( $b(SE) = -11.35 (7.06), p = .11$ ); however this link became significant when BMI and depressive symptoms were added as covariates to the model ( $b(SE) = -21.36 (7.91), p = .01$ ).

Separate regression analyses with change scores indexing reactivity (i.e., 30 minute post TSST – baseline) and recovery (i.e., 30 minute post-TSST - 75 minute post-TSST) indicated that early family stress was marginally related to smaller increases between baseline and peak cortisol ( $b(SE) = -.21 (.12), p = .08$ ) and smaller decreases between peak cortisol and the last

cortisol sample ( $b(SE) = .15 (.08)$ ,  $p = .07$ ). These associations became significant when BMI and depressive symptoms were included as covariates [reactivity change score: ( $b(SE) = -.38 (.13)$ ,  $p = .004$ ); recovery change score: ( $b(SE) = .22 (.09)$ ,  $p = .02$ ]

**HPA and inflammation.** Next, we examined the relation between the HPA axis and inflammation using multilevel growth curve modeling and regression analyses. The growth curve models were similar to that indicated in Equation 2, except that HPA parameters (i.e., AUCg, AUCi, reactivity and recovery change scores) were entered at Level 2. There was a significant time x AUCi interaction ( $p = .02$ ) and a marginally significant time<sup>2</sup> x AUCi interaction ( $p = .06$ ), as presented in Table 5. As depicted in Figure 5a, there was an accelerated increase in IL-6 for individuals who had higher cortisol AUCi [time:  $b(SE) = .04 (.04)$ ,  $p = .31$ ; time<sup>2</sup>:  $b(SE) = .03 (.01)$ ,  $p = .004$ ] compared to individuals with lower cortisol AUCi [time:  $b(SE) = -.03 (.04)$ ,  $p = .53$ ; time<sup>2</sup>:  $b(SE) = .04 (.01)$ ,  $p = .001$ ]. Levels of IL-6 at each time point did not significantly differ between individuals with high and low cortisol AUCi.

Using change scores to index reactivity yielded similar results [time:  $b(SE) = .09 (.04)$ ,  $p = .04$ ; time<sup>2</sup>: ( $b(SE) = -.03 (.01)$ ,  $p = .04$ ]. As shown in Figure 5b, there was an accelerated increase in IL-6 for individuals with higher cortisol reactivity change scores [time:  $b(SE) = .04 (.04)$ ,  $p = .27$ ; time<sup>2</sup>:  $b(SE) = .03 (.01)$ ,  $p = .001$ ] than those with smaller cortisol reactivity change scores [time:  $b(SE) = -.03 (.04)$ ,  $p = .58$ ; time<sup>2</sup>:  $b(SE) = .05 (.01)$ ,  $p < .001$ ]. Levels of IL-6 at each time point did not significantly differ between individuals with high and low change scores indicating cortisol reactivity.

There was also a marginally significant interaction between cortisol recovery change scores and time<sup>2</sup> ( $b(SE) = .03 (.02)$ ,  $p = .07$ ). As shown in Figure 5c, individuals who had smaller recovery change scores had increasingly greater IL6 responses to the TSST [time:  $b(SE) = .01$

(.04),  $p = .87$ ; time<sup>2</sup>:  $b(SE) = .04 (.01)$ ,  $p < .001$ ] than those with greater recovery change scores [time:  $b(SE) = .004 (.04)$ ,  $p = .92$ ; time<sup>2</sup>:  $b(SE) = .03 (.01)$ ,  $p = .01$ ]. Levels of IL-6 at each time point did not significantly differ between individuals with high and low cortisol recovery.

By contrast, in separate linear regression models with IL6 change scores as the outcome and cortisol AUCg, AUCi, and reactivity and recovery change scores as the predictor variables, there was no relation between the HPA axis and inflammation ( $p$ 's  $> .11$ ).

**Sympathetic nervous system.** A series of multi-level growth models and multiple regression models were conducted to test our hypothesis that early family stress would be related to enhanced SNS activity, which in turn would be related to greater inflammation.

**Early family stress and SNS functioning.** To examine whether sAA and cortisol responses varied as a function of early family stress, a model similar to that indicated in Equation 2 was tested. In this model, sAA was the outcome variable and BMI was excluded as a covariate. As presented in Table 6 and Figure 6, we found that early family stress was not associated with sAA at baseline ( $p = .12$ ) and in response to the TSST (time:  $p = .17$ ; time<sup>2</sup>:  $p = .14$ ).

Consistently, multiple regression models in which sAA AUCg, AUCi, and reactivity and recovery changes scores were regressed on early family stress showed that RF scores were not related to total AUCg ( $b(SE) = -13.50 (12.03)$ ,  $p = .27$ ), AUCi ( $b(SE) = 5.39 (5.92)$ ,  $p = .37$ ), reactivity change scores ( $b(SE) = .06 (.11)$ ,  $p = .58$ ), and recovery change scores ( $b(SE) = -.09 (.10)$ ,  $p = .38$ ).

**SNS and inflammation.** We next tested whether SNS and inflammatory activity were related using both multilevel growth curve modeling and regression analyses. For multilevel growth curve modeling, we tested similar models that were similar to that indicated in Equation 2, except that we replaced RF scores with SNS parameters (AUCg, AUCi, reactivity and

recovery change scores). Overall, we found no relation between sAA activity and inflammatory reactivity. Specifically there were no significant interactions between sAA AUCg, AUCi, and reactivity change scores and time and time<sup>2</sup> ( $p$ 's > .31). Similarly, in regression analyses, SNS indices did not predict increases in IL-6 ( $p$ 's > .18).

**Sleep.** A series of multiple regressions were conducted to test our hypothesis that early family stress would be related to poorer sleep, which in turn would be related to greater inflammation.

**Early family stress and sleep.** Early family stress was not related to measures of daily sleep parameters, including latency, duration, and efficiency ( $p$ 's = .80-96). However, early family stress was related to several dimensions of sleep as measured by the PSQI. As shown in Table 7, higher scores on the RF questionnaire were related to poorer overall sleep ( $p$  = .03), and greater sleep disturbance ( $p$  = .03) and day dysfunction due to sleepiness ( $p$  < .001). Higher RF scores were also marginally related longer sleep latency ( $p$  = .07). However, only the association between RF scores and day dysfunction due to sleepiness remained significant upon adjusting for depressive symptoms ( $b(SE)$  = .36 (.15),  $p$  = .02). Consistent with the daily measures of sleep duration and sleep efficiency, RF scores were unrelated to PSQI measures of sleep duration ( $p$  = .95) and efficiency ( $p$  = .45).

**Sleep and inflammation.** Both multi-level growth curve and multiple regression models were used to examine the association between sleep parameters that were related to early family stress and inflammation. In growth curve models, we found a significant cross-level interaction between PSQI sleep latency and time ( $b(SE)$  = .07 (.03),  $p$  = .05) and a marginally significant interaction between PSQI sleep latency and time<sup>2</sup> ( $b(SE)$  = -.02 (.01),  $p$  = .06). Follow up tests of simple slopes using mean splits indicated an accelerated increase of IL-6 for individuals with

longer sleep latency: [time:  $b(SE) = -.08 (.04)$ ,  $p = .05$ ; time<sup>2</sup>:  $b(SE) = .06 (.01)$ ,  $p < .001$ ] compared to individuals with shorter sleep latency [time:  $b(SE) = .06 (.04)$ ,  $p = .09$ ; time<sup>2</sup>:  $b(SE) = .02 (.01)$ ,  $p = .05$ ]. However, as depicted in Figure 7, this was due to higher levels of baseline IL-6 among individuals with longer sleep latency. There were no cross-level interactions between the other sleep parameters and time ( $p$ 's  $> .39-.74$ ) and time<sup>2</sup> ( $p$ 's  $> .35-.91$ ). In regression analyses, sleep parameters were unrelated to IL-6 at baseline ( $p = .12-.69$ ) and reactivity change scores ( $p = .12-.74$ ).

### **Early Family Stress, Psychosocial Processes, and Inflammation (Primary Aim 3)**

The third aim of the study was to investigate whether early family stress was associated with difficulties in psychosocial processes, and whether these in turn influenced inflammatory processes. We specifically hypothesized that higher RF scores would be related to higher threat appraisals of the TSST, greater negative emotional reactivity to the TSST, and poorer social relationships.

**Early family stress, threat appraisals, and inflammation.** Overall, participants found the task and confederates to be threatening (see Table 1 for descriptives). Multiple regression analyses indicated that as hypothesized, individuals from riskier families appraised the TSST as more threatening. More specifically, individuals who had higher RF scores tended to have higher anticipatory threat appraisals ( $p = .03$ ; Table 8, column 1) as well as higher retrospective threat appraisals ( $p < .001$ ; Table 8, column 2). Although more depressive symptoms were related to higher threat appraisals (see Table 2d), adjusting for depressive symptoms did not alter results (anticipatory threat appraisals:  $b(SE) = .11 (.05)$ ,  $p = .04$ ; retrospective threat appraisals:  $b(SE) = .28 (.12)$ ,  $p = .02$ ). Anticipatory and retrospective threat appraisals, in turn, were unrelated to

IL-6 at baseline and in response to the TSST in growth curve models ( $p$ 's > .14) and in multiple regression models ( $p$ 's > .46).

**Early family stress, emotional response, and inflammation.** The TSST generally increased NA in participants, albeit only slightly (see Table 1 for descriptives). Multiple regression models showed that contrary to hypotheses, RF scores were not related to overall NA reactivity to the TSST ( $p = .81$ ), as presented in Table 9 (column 1). However, when depressive symptoms were added to the model, a significant relation emerged, such that individuals experiencing early family stress tended to have smaller increases in NA in response to the TSST ( $b(SE) = -.27 (.12)$ ,  $p = .02$ ).

Because NA encompasses different emotions, some of which may be more relevant to TSST, we examined whether early adversity was related to any of the subscales of the PANAS-X. As depicted in Table 9, higher RF scores were not related to any of the subscales. However, when controlling for depressive symptoms, RF scores were related to smaller increases in anger ( $b(SE) = -.32 (.14)$ ,  $p = .02$ ) and guilt ( $b(SE) = -.41 (.16)$ ,  $p = .01$ ) in response to the TSST. RF scores were not associated with reactivity of fear and sadness ( $p$ 's > .50) when adjusting for depressive symptoms. In turn, none of the measures of emotional reactivity interacted with time to predict IL6 in growth curve models ( $p$ 's = .27-.96), and in regression models, affect reactivity measures did not predict IL-6 increases ( $p$ 's = .13-.99).

**Social relationships.** Lastly, we examined the association between early adversity and social relationships, hypothesizing that more early family stress would be associated with poorer quality relationships. Overall participants reported having relatively good relationships (see Table 1 for descriptives). Multiple regression models showed that individuals who reported growing up in a riskier family tended to have less supportive relationships ( $p < .001$ ), as shown

in Table 10. This association remained significant even when controlling for depressive symptoms ( $b(SE) = -.16 (.06), p = .01$ ).

Because social relationships are multi-faceted, we examined the relation between early family stress and scores on the subscales of the SPS. We found that higher RF score were significantly related to all the dimensions of supportive relationships with the exception of nurturance, as shown in Table 10. However, when controlling for depressive symptoms, only the links between early family stress and reassurance of worth ( $b(SE) = -.31 (.09), p = .001$ ) and tangible support ( $b(SE) = -.24 (.08), p = .002$ ) remained statistically significant. The link between early family stress and emotional closeness ( $b(SE) = -.18 (.10), p = .06$ ) and informational support ( $b(SE) = -.17 (.10), p = .08$ ) became marginally significant, and the link to social integration became non-significant ( $b(SE) = -.12 (.10), p = .22$ ).

In turn, none of the dimensions of supportive relationships interacted with time to predict IL6 ( $p$ 's = .40-.96) in growth curve models. In multiple regression models, higher overall SPS scores were marginally related to smaller IL-6 increases ( $b(SE) = -.18 (.10), p = .08$ ), and higher tangible support was significantly related to smaller IL-6 increases ( $b(SE) = -.18 (.07), p = .04$ ). However, these links became non-significant when controlling for depressive symptoms.

### **Psychosocial Functioning and HPA axis and SNS Responses to Stress (Secondary Aim)**

Although not part of the primary purpose of the study, we examined whether any of the psychosocial factors were related to HPA and sAA reactivity given that both theoretical and empirical work suggests that cognitive appraisals, emotional reactivity, and social relationships are related to HPA and SNS responses to stress. Because repeated assessments were nested within individuals, analyses were conducted using multi-level growth curve modeling. A series

of models similar to that in Equation 2 were tested with cortisol or sAA as the outcome variable and each of the psychosocial parameters entered in Level 2.

**Appraisals.** In separate models, we examined whether anticipatory and retrospective threat appraisals modulated the relation between time and cortisol and sAA. We found a significant interaction between anticipatory threat appraisals and time ( $b(SE) = -.26 (.11)$ ,  $p = .02$ ) and time<sup>2</sup> ( $b(SE) = .05 (.02)$ ,  $p = .01$ ). As depicted in Figure 8a, individuals with greater anticipatory threat appraisals tended to have dampened cortisol responses [time:  $b(SE) = .20 (.05)$ ,  $p < .001$ ; time<sup>2</sup>:  $b(SE) = -.05 (.01)$ ,  $p < .001$ ] compared to those with lower anticipatory threat appraisals (below mean) [time:  $b(SE) = .30 (.04)$ ,  $p < .001$ ; time<sup>2</sup>:  $b(SE) = -.06 (.01)$ ,  $p < .001$ ]. A similar pattern emerged with retrospective threat appraisals. Retrospective threat appraisals significantly interacted with time ( $b(SE) = -.16 (.05)$ ,  $p = .001$ ) and time<sup>2</sup> ( $b(SE) = .02 (.01)$ ,  $p = .003$ ). As depicted in Figures 8b, individuals perceiving greater threat after the TSST tended to have dampened cortisol activity [time:  $b(SE) = .19 (.05)$ ,  $p < .001$ ; time<sup>2</sup>:  $b(SE) = -.05 (.01)$ ,  $p < .001$ ] compared to those who perceived less threat [time:  $b(SE) = .31 (.03)$ ,  $p < .001$ ; time<sup>2</sup>:  $b(SE) = -.06 (.01)$ ,  $p < .001$ ]. Threat appraisals did not interact with time to influence sAA responses to the TSST ( $p$ 's = .27-.84).

**Emotional reactivity.** Growth curve models with NA reactivity entered at Level 2 revealed that cortisol responses also varied by NA reactivity to the TSST. In particular, there were significant cross-level interactions between NA reactivity and time ( $b(SE) = .11 (.05)$ ,  $p = .02$ ) and a marginally significant interaction with time<sup>2</sup>: ( $b(SE) = -.02 (.01)$ ,  $p = .06$ ). As shown in Figure 9a, greater emotional reactivity was associated with greater cortisol activity [time:  $b(SE) = .32 (.05)$ ,  $p < .001$ ; time<sup>2</sup>:  $b(SE) = -.06 (.01)$ ,  $p < .001$ ] compared to less emotional reactivity [time:  $b(SE) = .24 (.04)$ ,  $p < .001$ ; time<sup>2</sup>:  $b(SE) = -.05 (.01)$ ,  $p < .001$ ].

We also examined whether any of the PANAS subscales modulated cortisol responses and found significant interactions between fear reactivity and time ( $b(SE) = .10 (.03), p = .002$ ) and time<sup>2</sup> ( $b(SE) = -.01 (.01), p = .02$ ). Greater fear activity was associated with greater cortisol activity [time:  $b(SE) = .40 (.05), p < .001$ ; time<sup>2</sup>:  $b(SE) = -.08 (.01), p < .001$ ] compared to less fear reactivity [time:  $b(SE) = .19 (.03), p < .001$ ; time<sup>2</sup>:  $b(SE) = -.05 (.01), p < .001$ ], as presented in Figure 9b. Likewise, there were also significant interactions between guilt reactivity and time ( $b(SE) = .08 (.03), p = .03$ ) and time<sup>2</sup> ( $b(SE) = -.01 (.01), p = .03$ ). Greater guilt reactivity was associated with heightened cortisol activity [time:  $b(SE) = .29 (.05), p < .001$ ; time<sup>2</sup>:  $b(SE) = -.06 (.01), p < .001$ ] compared to less guilt reactivity [time:  $b(SE) = .26 (.04), p < .001$ ; time<sup>2</sup>:  $b(SE) = -.05 (.01), p < .001$ ], as shown in Figure 9c. Measures of emotional reactivity did not modulate sAA responses to the TSST ( $p$ 's = .19-.99).

**Social relationships.** There were no interactions between overall SPS scores and time and time<sup>2</sup> on cortisol responses to the TSST. However, when examining whether cortisol responses varied according to scores on the SPS subscales, we found significant interactions between emotional closeness and time ( $b(SE) = -.11 (.04), p = .04$ ) and time<sup>2</sup> ( $b(SE) = .02 (.01), p = .04$ ). As depicted in Figure 10a, individuals perceiving less emotional closeness in their relationships tended to exhibit attenuated cortisol reactivity to the TSST [time:  $b(SE) = .22 (.04), p < .001$ ; time<sup>2</sup>:  $b(SE) = -.05 (.01), p < .001$ ] than individuals perceiving more emotional closeness [time:  $b(SE) = .33 (.04), p < .001$ ; time<sup>2</sup>:  $b(SE) = -.07 (.01), p < .001$ ]. There were also significant interactions between tangible support and time ( $b(SE) = .26 (.07), p < .001$ ) and time<sup>2</sup> ( $b(SE) = -.05 (.01), p < .001$ ). Cortisol responses to the TSST were dampened for those perceiving less tangible support [time:  $b(SE) = .19 (.05), p < .001$ ; time<sup>2</sup>:  $b(SE) = -.04 (.01), p < .001$ ] compared to those perceiving more tangible support [time:  $b(SE) = .32 (.04), p < .001$ ;

time<sup>2</sup>:  $b(SE) = -.06 (.01)$ ,  $p < .001$ ]. Parallel multilevel growth curve models with sAA as the outcome variable indicated that social relationships did not modulate SNS responses to the TSST.

### **Gender, Ethnicity, and Subtypes of Early Family Stress (Exploratory Aims)**

**Gender.** Gender moderation analyses were conducted to examine whether the effects of early family stress on biological systems and psychosocial factors differed between males and females. Results from this set of analyses indicated that gender did not moderate any of the associations between early family stress and inflammation, sleep, and HPA, SNS, and psychosocial functioning.

**Ethnicity.** We also conducted ethnicity moderation analyses to determine whether the effects of early family stress differed between European- and Latin- Americans. We found that ethnicity moderated the association between early family stress and cortisol in multilevel growth curve models [rf x ethnicity x time:  $b(SE) = -.30 (.12)$ ,  $p = .01$ ; rf x ethnicity x time<sup>2</sup>:  $b(SE) = .06 (.02)$ ,  $p = .01$ ]. The interactions between early family stress and time was only significant among Latinos [time:  $b(SE) = -.22 (.06)$ ,  $p < .001$ ; time<sup>2</sup>:  $b(SE) = .04 (.01)$ ,  $p < .001$ ] and not among European-Americans [time:  $b(SE) = .07 (.08)$ ,  $p = .38$ ; time<sup>2</sup>:  $b(SE) = -.02 (.01)$ ,  $p = .27$ ].

For psychosocial variables, multiple regression analyses revealed a significant interaction between RF scores and ethnicity on anger reactivity ( $b(SE) = .80 (.32)$ ,  $p = .02$ ). Among European-Americans, higher RF scores were associated with decreased anger reactivity to the TSST ( $b(SE) = -.74 (.29)$ ,  $p = .01$ ). The early family stress-anger reactivity link was non-significant for Latino Americans ( $b(SE) = .05 (.14)$ ,  $p = .70$ ).

There was also a significant early family stress by ethnicity interaction on the SPS ( $b(SE) = -.29 (.15)$ ,  $p = .05$ ). Higher RF scores were related to less supportive relationships overall

among Latinos ( $b(SE) = -.31 (.06)$ ,  $p < .001$ ), but not among European Americans ( $b(SE) = -.02 (.13)$ ,  $p = .90$ ). When examining the subscales of the SPS, we found that RF scores interacted with ethnicity only for the informational support subscale ( $b(SE) = -.49 (.22)$ ,  $p = .03$ ). Higher RF scores were related to less informational support among Latinos ( $b(SE) = -.36 (.10)$ ,  $p < .001$ ), but not among European Americans ( $b(SE) = .13 (.20)$ ,  $p = .52$ ).

**Family stressor subtype.** Given a burgeoning literature on distinct effects of different types of early adversity, we also explored the unique effects of different types of early family stress. Following previous research (Crosswell et al., 2014), we created three subscales from the RF questionnaire, including neglect, abuse, and a chaotic home environment. In this set of analyses, neglect, abuse, and a chaotic home environment were entered simultaneously in all models. Findings showed that different types of stressors have differential effects on biobehavioral and psychosocial processes.

**Neglect.** Experiences of neglect were uniquely associated with cortisol responses to the TSST. There was a significant interaction between neglect and time  $b(SE) = -.12 (.03)$ ,  $p < .001$ ) and time<sup>2</sup>  $b(SE) = .02 (.01)$ ,  $p < .001$ ). Neglect was also significantly associated with sleep quality as assessed by the PSQI, such that more neglect was related to better sleep quality ( $b(SE) = -.19 (.10)$ ,  $p = .03$ ).

For psychosocial factors, more neglect experienced during early life was associated with significantly higher retrospective threat appraisals ( $b(SE) = .19 (.09)$ ,  $p = .05$ ). This link became marginal when adjusting for depressive symptoms ( $b(SE) = .16 (.09)$ ,  $p = .07$ ). More neglect was also associated with greater reactivity of sadness ( $b(SE) = .26 (.09)$ ,  $p = .01$ ), and less supportive relationships overall ( $b(SE) = -.12 (.05)$ ,  $p = .02$ ), informational support ( $b(SE) = -.19 (.07)$ ,  $p = .01$ ), and tangible support ( $b(SE) = -.25 (.05)$ ,  $p < .001$ ).

**Abuse.** Early experiences of abuse were only associated with sleep above and beyond experiences of neglect and a chaotic home environment. More specifically, more frequent experiences of abuse were related to worse overall sleep ( $b(SE) = 1.02 (.43)$ ,  $p = .02$ ) and greater dysfunction during the day due to sleepiness ( $b(SE) = .25 (.08)$ ,  $p = .004$ ).

**Chaos.** A chaotic home environment was associated with emotional reactivity to the TSST and social relationships. In particular, a more chaotic home environment was related to decreased reactivity of guilt ( $b(SE) = -.32 (.15)$ ,  $p = .04$ ). When adjusting for depressive symptoms, we also found that a more chaotic home environment was related to decreased reactivity of overall NA ( $b(SE) = .21 (.12)$ ,  $p = .04$ ). Interestingly, a chaotic home environment was also related to higher levels of opportunity for nurturance ( $b(SE) = -.21 (.10)$ ,  $p = .05$ ). A more chaotic home environment was also related to lower levels of informational support ( $b(SE) = -.19 (.09)$ ,  $p = .03$ ) and reassurance of worth ( $b(SE) = -.17 (.08)$ ,  $p = .05$ ), although these associations became non-significant when depressive symptoms were added to the model [informational support:  $b(SE) = -.15 (.09)$ ,  $p = .10$  reassurance of worth:  $b(SE) = -.13 (.09)$ ,  $p = .12$ ].

## Discussion

Research has documented an association between early family stress and heightened inflammation, but few studies have focused on younger samples and inflammatory reactivity, and pathways are incompletely understood. Thus, the overarching goal of the current study was to examine the contributions of early family stress to inflammatory reactivity to stress and the underlying biobehavioral and psychosocial mechanisms among late adolescents. We found that early family stress was not related to inflammatory reactivity, contrasting previous work showing a link between early family stress and higher baseline levels of inflammation. This finding

precluded tests of mediation by disruptions in biobehavioral and psychosocial functioning.

Nevertheless, we did find that early family stress was related to dampened cortisol responses to stress, poorer sleep, higher threat appraisals, and less supportive relationships. These findings support key pieces of the Risky Families and Biological Embedding Models (Miller et al., 2011; Repetti et al., 2002).

Overall, we found little support for models positing that disruptions in biological stress systems and psychosocial processes mediate the link between early family stress and inflammation and poor health (Miller et al., 2011; Repetti et al., 2002). Why we found little support for these models is not entirely clear. Of note, however, is the low level of early family stress in the current sample. The average RF score in the present study was 1.92, which indicates that family-related stressors included in the RF questionnaire rarely occurred. It may be that more severe or chronic levels of early family adversity more profoundly impact biological systems and psychosocial functioning to give rise to exaggerated inflammatory reactivity. We may not have been able to recruit individuals experiencing more early family stress because laboratory sessions occurred at UCLA, which was up to a 3-hour round-trip commute for participants of the larger Family Health Study, from which participants of the current study were drawn. Individuals with more early family stress may not have had the time or resources to participate in the present study. A number of other issues may have also contributed to findings for specific pieces of the model, as discussed below.

### **Early Adversity and Inflammation (Primary Aim 1)**

We hypothesized that early family stress would be related to higher levels of IL-6 at baseline and in response to acute social stress. In the present study we found no evidence for a link between early family stress and inflammation at baseline and in response to stress. These

null findings contrast the growing literature documenting a link between early adversity and higher levels of baseline inflammation (Baumeister, Akhtar, Ciufofolini, Pariente, & Mondelli, in press). A number of factors may help explain the divergent findings. First, previous studies have largely examined the effects of socioeconomic disadvantage and severe forms of early family stress such as physical and sexual abuse (Miller et al., 2011). In the present study, we examined overall harshness of the family environment using the RF questionnaire, and as noted above, participants reported experiencing low levels of early family stress. Low levels of early family-related stress may reflect typical variation in early family stress. Given that the current sample was young and healthy, and levels of inflammation are low during development, it may be that only more severe forms of early family stress impact inflammatory activity that can be observed during late adolescence.

To our knowledge, only three past studies focusing on inflammation have used the RF questionnaire. One study found that higher RF scores were related to higher levels of IL-6, but this was in a sample of breast cancer survivors and the link was attenuated when adjusting for depressive symptoms and current stress (Crosswell et al., 2014). Another study found that only physical abuse items from the RF questionnaire were related to higher levels of inflammation, a finding we did not observe in the present study. However, participants in this study were 32-47 years-old (Carroll et al., 2013). By contrast, the third study was of adolescents and researchers of this study found no relation between RF scores and baseline levels of inflammation (Miller & Chen, 2010), which is similar to the present findings. Of note is that the former two studies focused on adults whereas the latter study and the present study focused on adolescents.

It is possible that the early adversity does increase inflammation, but that its effects on baseline circulating levels of inflammation may not manifest until later in life. If so, the effects

of early family stress on inflammation in younger samples may be more apparent when the inflammatory system is challenged. Indeed, past studies have found that family-related stress predicts exaggerated production of inflammation in response to bacterial challenge among adolescents (e.g., Miller et al., 2009). By contrast, our findings suggest that early adversity is not related to inflammation when inflammatory processes are challenged psychosocially. Circulating inflammatory cytokines in response to stress may stem from both immune and non-immune cells such as adipose cells. The link between early adversity and inflammation in young samples may be evident only when using deeper measures of inflammation that specifically probe immune cells.

Alternatively, the inflammatory effects following early family stress in younger samples may be evident in the context of vulnerability and negative lifestyle factors. For instance, in a longitudinal study, contemporaneously measured early family stress (i.e., maternal psychopathology, harsh discipline, family income, parental criminal behavior) was not directly related to inflammation at 22-25 years of age; instead, early family stress was indirectly related to higher levels of inflammation via smoking and adiposity (Raposa, Bower, Hammen, Najman, & Brennan, 2014). Early adversity increases the risk for adiposity (Midei & Matthews, 2011) and cigarette smoking (Topitzes, Mersky, & Reynolds, 2009), which are known to stimulate inflammation. Individuals who experience early adversity and engage in negative health behaviors may exhibit early emergence of the early adversity-inflammation link.

Yet another possibility is that contemporaneous interpersonal stressors may matter more for inflammatory reactivity among developing youth and late adolescents. Some prior work suggests that adolescents may be more sensitive to their social environment (Blakemore & Mills,

2014; Somerville, 2013). Based on this notion, more proximal stressors such as those in daily life might increase inflammatory responses to a subsequent negative social interaction.

### **Early Family Stress, Biobehavioral Processes, and Inflammation (Primary Aim 2)**

Based on theoretical models (e.g., Miller et al., 2011, Repetti et al., 2002; McEwen, 1998), we had hypothesized that greater early family stress would be related to alterations in HPA and SNS responses to stress and disruptions in sleep, which in turn would be related to heightened inflammatory reactivity. Overall, we found partial support for these hypotheses. More specifically, we found that early family stress was related to dampened cortisol activity and to more sleep-related problems, particularly to higher levels of day dysfunctioning due to sleepiness. By contrast, we found that early family stress was unrelated to sAA activity. In turn, only HPA responses were related to inflammatory responses.

**HPA axis.** The link between early family stress and dampened cortisol reactivity and recovery to the TSST in the present study has also been observed in prior work (e.g., Dietz et al., 2013; Fernald et al., 2008; Carpenter et al., 2009). However, some previous work has revealed a positive association between early family stress and heightened HPA activity (e.g., Engert et al. 2010; Kumari et al. 2012). A possible explanation for the present finding is that growing up in an overall harsh family environment places youth in a state of constant stress, leaving little room for adequate recovery (Miller, Chen, & Zhou, 2007; Repetti et al., 2002). Repeated or ongoing stress can result in repeated or sustained HPA activation, leading to high levels of cortisol, which can have detrimental effects on the developing brain, health, and behavior (Kapoor, Petropoulos, & Matthews, 2008; Lupien, McEwen, Gunnar, & Heim, 2009). To minimize these negative effects, the body may recalibrate the HPA axis to downregulate even in the face of stress (Del Giudice, Ellis, & Shirtcliff, 2011). Alternatively, high levels of glucocorticoids may contribute to reduced

sensitivity of the various components of the HPA axis. Thus, blunted HPA activity in relation to early family stress may also reflect disruptions in the ability to mount an HPA response. The current data are unable to test these hypotheses, and therefore, these explanations remain speculative at this time.

Increased cortisol reactivity, as measured by cortisol AUCi and change scores, was related to greater increases of IL-6 over time. Because change scores do not necessarily reflect absolute levels of cortisol, this positive association may reflect individual differences in sensitivity to acute stress. Individuals who exhibited greater activation of the HPA axis also exhibited greater IL-6 increases. We also found that lower cortisol recovery change scores were marginally related to greater IL-6 increases over the course of the experimental session. Given that cortisol has anti-inflammatory effects, this inverse association of decreased HPA activity and enhanced inflammatory reactivity are consistent with prior work documenting the anti-inflammatory effects of glucocorticoids. This association may be stronger when examining the relation between inflammation and absolute levels of cortisol. Ultimately, the effects of cortisol on inflammatory processes may depend on sensitivity of glucocorticoid receptors in immune cells, which was not assessed in the present study.

**SNS.** We found no evidence that early family stress leads to exaggerated SNS reactivity or prolonged recovery, and that SNS activity contributes to inflammatory reactivity. This finding contrasts theoretical models positing that one pathway by which early adversity increases risk for poor health outcomes is via dysregulated SNS stress responses (Repetti et al., 2002). Of note is that the literature on early family stress and SNS activity consists of mixed results. Studies of youth that rely on impedance cardiography to assess SNS activation have consistently shown that early family stress is related to enhanced SNS activity (e.g., El-Sheikh, 2005; Ellis et al., 2005;

Oosterman et al., 2010). By contrast, studies assessing SNS activity via sAA have yielded inconsistent findings (e.g., Hill-Soderlund et al., 2015; Taylor et al., 2013) with some studies indicating no relation between early family stress and sAA (Keeshin et al., 2015), as in the present study. Similarly, studies assessing cardiovascular activity, which is correlated with SNS activity, have also yielded mixed findings (Gatt et al., 2009; Lovallo, 2013).

These mixed findings in past work as well as the present null findings for early family stress, SNS activity, and inflammation may be explained by differences in SNS measurement. Cardiovascular activity, although correlated with SNS activity, also reflects parasympathetic activity. Likewise, although sAA has been previously thought to be an indicator of SNS activation (Nater & Rohleder, 2009), it has been found to be only moderately correlated with catecholamine responses to stress (Nater & Rohleder, 2009). Furthermore, sAA responses to stress may not be completely independent of parasympathetic control of saliva flow rate and may therefore also reflect activity of both the sympathetic and parasympathetic branches of the autonomic nervous system (J. A. Bosch, Veerman, de Geus, & Proctor, 2011). Purer measures of SNS activation come from impedance cardiography. It may be that early family stress does affect SNS activity, which then influences inflammatory activity as proposed by theoretical models (Miller et al., 2011; Repetti et al., 2002), but we were unable to capture these links perhaps given our measure of SNS activation.

**Sleep.** Consistent with our hypothesis about sleep, early family stress was related to poorer overall sleep, more sleep disturbance, and greater day dysfunction due to sleepiness. These findings align with previous studies showing positive associations between early adversity and sleep problems (Kajepeta et al. 2015). The relations between early family stress and total sleep and sleep disturbance were attenuated and became non-significant in models controlling for

depressive symptoms. This suggests that early family stress may influence these aspects of sleep by increasing depressive symptoms. This is in line with past research showing that childhood abuse increases sleep problems through increasing risk for psychopathology, including anxiety, depression, posttraumatic stress, anger, and dissociation (Cecil, Viding, McCrory, & Gregory, 2015; Gelaye et al., 2015).

Interestingly, the relation between early family stress and day dysfunction due to sleepiness remained statistically significant even when depressive symptoms were added to the model. This suggests that early family stress may influence day dysfunction via other pathways. Other studies have similarly found that early family stress is related to feeling tired even after a good night's sleep (Chapman, Wheaton, et al., 2011) and daytime dysfunction (Sansone, Edwards, & Forbis, 2010). However, many other studies have found that early family stress is related to other aspects of sleep as well (Glod et al., 1997; El-Sheikh et al., 2006). Why early family stress was related to day dysfunction above and beyond depressive symptoms remains unclear.

In turn, daytime dysfunction due to sleepiness was unrelated to inflammation. Despite a growing literature demonstrating sleep as a critical contributor to inflammatory processes, we found that only longer sleep latency as assessed by the PSQI was related to greater increases in IL-6. However, upon further examination, we found that this was driven by lower levels of IL-6 at baseline among those with longer sleep latency. The overall lack of findings for sleep and inflammation seems to contrast previous work, but the majority of past studies focus on adults. Only a handful of studies have examined the relationship between sleep and inflammation among adolescents and have yielded mixed findings. An earlier study found that shorter sleep duration assessed via actigraphy was related to higher levels of CRP (E. K. Larkin et al., 2005).

By contrast, two more recent studies did not find an overall relation between actigraphy sleep duration and CRP. Instead, they found the sleep duration-inflammation link to be conditional on other factors. One study found that shorter actigraphy sleep duration only during weekdays was related to higher CRP (Hall, Lee, & Matthews, 2015). Another study found that shorter sleep duration assessed by actigraphy was related to higher levels of CRP only among adolescents younger than 16.4 years old (Park et al., 2016). Together, these findings suggest that the sleep-inflammation link during adolescents may be conditional and better observed using behavioral measures of sleep (e.g., actigraphy).

### **Early Family Stress, Psychosocial Processes, and Inflammation (Primary Aim 3)**

We had hypothesized that greater early family stress would be related to alterations in psychosocial functioning, which in turn, would predict enhanced inflammatory reactivity. In partial support of these hypotheses, we found that early family stress was related to higher threat appraisals and less supportive relationships. Contrary to hypotheses, we found that early family stress was related to decreased NA reactivity. In turn, psychosocial factors were unrelated to inflammatory reactivity.

**Cognitive appraisals.** Given past empirical and theoretical work, we hypothesized that more early family stress would be related to higher threat appraisals (Miller et al., 2011), which in turn, would contribute to heightened inflammatory reactivity (Denson, Spanovic, & Miller, 2009; O'Donovan et al., 2012). Consistent with hypotheses, we found that individuals with greater exposure to early family stress tended to appraise the laboratory stressor as more threatening. However, we found that threat appraisals did not contribute to inflammatory responses to stress.

The positive association between early family stress and threat appraisals observed in the

present study is consistent with past literature (e. g., Miller et al., 2011; Tottenham et al., 2011). However, the disconnect between cognitive appraisals and inflammatory processes observed in the present study seems to contrast previous literature. Few studies have directly examined the role of threat appraisals in inflammatory responses to threat. Nevertheless, these studies have found that higher threat appraisals are related to heightened stimulated production of inflammatory cytokines in youth with asthma (Chen et al., 2006), as well as male adults (Wirtz et al., 2007). These studies involved small samples of youth with asthma and adult men. Thus, participant characteristics may have contributed to different findings. Assessment of inflammation may have also been a source of variation. These past studies focused on stimulated immune cells with LPS, and in the present study, we examined inflammatory reactivity to psychosocial stress, which yields much smaller increases in inflammation. Of course, it is also possible that cognitive appraisals may have minimal influence on inflammatory processes in the present sample. Given the paucity of research on cognitive appraisals and inflammation, the role of threat appraisals in the stress-inflammation link remains unclear.

**Emotional reactivity.** We hypothesized that early family stress would be related to exaggerated emotional reactivity to the TSST, and that this heightened emotional reactivity would contribute to heightened inflammatory responses. Contrary to hypotheses, we found that early family stress was related to smaller increases of general NA and anger. We also found that emotional reactivity was unrelated to inflammatory responses.

The current findings on early family stress and NA and anger reactivity contrast previous research showing that individuals experiencing early adversity tend to exhibit heightened negative emotional responses (Miller et al., 2011; Repetti et al., 2002). However, some adversity is thought to be beneficial, as it facilitates development of resources of dealing with subsequent

adversity (Seery, 2011). In light of the relatively low levels of early family stress in the present sample, it may be that some early family stress is actually beneficial for emotion processing.

Why emotional reactivity did not predict inflammatory reactivity in the present study also remains unclear. Past work has associated more negative emotions to greater inflammation (e.g., Carroll et al., 2011; Howren et al., 2009), which seems to contrast the our findings. However, the majority of past work has primarily assessed global or trait level negative emotions such as anxiety, anger, or depression (Howren et al., 2009; O'Donovan et al., 2012; Marsland et al., 2008) and baseline levels of inflammation. In this study, we focused on emotional and inflammatory reactivity to an acute stressor. Emotional and inflammatory responses to specific situations may function differently from more chronic, baseline levels of negative emotion and inflammation.

Only a handful of studies have examined emotional and inflammatory responses to an acute stressor, showing a positive association between emotional and inflammatory responses. One study found that anger and anxiety responses to the TSST were associated with great IL-6 responses (Carroll et al., 2011). A recent study found that anger reactivity to the TSST was also related to greater increases in IL-6, but only among individuals with low social support (Puterman et al., 2014). These studies were conducted on mid-life adults, and emotion and inflammatory processes are known to vary across developmental stages (Blakemore & Mills, 2014; O'Connor et al., 2009). Two studies of undergraduate students showed that anger was unrelated to inflammatory responses; instead, anxiety and fear responses were related to increases in inflammation (Moons et al., 2010; Moons & Shields, 2015). These studies suggest that particular negative emotions might differentially relate to inflammatory activity, which we

did not observe in the present study. This may be due to the fact that that these studies assessed inflammation via oral fluids, which may not reflect peripheral inflammatory processes.

Another possible explanation for why did not find a link between emotional and inflammatory responses is that negative emotional responses to stress may not always elicit an inflammatory response. Other factors contributing to the experiences and response to stress, such as emotion regulation, coping resources, and features of the stressors may contribute to how emotional responses impact inflammatory responses. More work is needed to address these questions.

**Social relationships.** We had expected that early family stress would be associated with poor social relationships, which would mediate the link between early family stress and heightened inflammatory reactivity. In partial support of our hypotheses, early family stress was related to less supportive relationships, but less supportive relationships were not related to inflammatory reactivity.

The inverse association between early family stress and overall quality of social relationships is consistent with past research (Luecken et al., 2013; Repetti et al., 2002). When probing specific aspects of social relationships that early family stress may have a particularly profound effect, we found that early family stress was related to lower levels of emotional closeness, reassurance of worth, tangible support, informational support, and social integration. Early family stress was only unrelated to opportunity for nurturance. However, when depressive symptoms were included as a covariate, many of these relations became attenuated. Only the links with reassurance of worth and tangible support remained significant.

This suggests that early family stress may strain quality of relationships, particularly emotional closeness, informational support, and social integration, by increasing the risk for

depressive symptoms. Numerous epidemiological and clinical studies have established that early family stress, ranging from maltreatment to parenting styles, increases for depression among throughout the lifespan (Hazel, Hammen, Brennan, & Najman, 2008; Heider, Matschinger, Bernert, Alonso, & Angermeyer, 2006; Heim & Binder, 2012). Depressed individuals as well as those vulnerable to depression are, in turn, more likely to generate stressors, particularly those interpersonal in nature (Hammen, 1991). This may be due to individual characteristics and behaviors, such as negative cognitive styles (Krackow & Rudolph, 2008; Liu & Alloy, 2010). The present findings suggesting mediation of early family stress on poor social relationships by depressive symptoms are consistent with prior work.

Overall quality of social relationships was unrelated to IL-6 responses to the TSST. With the exception of tangible support, each dimension of supportive relationships was also unrelated to changes in IL-6. However, the inverse relation between tangible support and IL-6 reactivity became non-significant when controlling for depressive symptoms. Overall, these findings suggest that having supportive relationships does not influence IL-6 reactivity to acute stress. These findings seem inconsistent with prior working showing that negative social interactions, loneliness, hostility, and a lack of social support and social connection enhances inflammatory reactivity (Chiang et al., 2012; Fuligni et al., 2009; J. Gouin, Glaser, Malarkey, Beversdorf, & Kiecolt-Glaser, 2012; Jaremka et al., 2013; John-Henderson et al., 2015; Kiecolt-Glaser et al., 2005). The relatively high levels of social support observed in the present sample may have contributed to our null findings. It is possible that the effects of poor social relationships on inflammatory responses to stress are observed only at lower extremes.

Differences in participant characteristics and methodology between the present and past studies may also contribute to the divergent findings. Many past studies focusing on

inflammatory reactivity have examined inflammatory markers from blood in mid-life and older adults or married couples (e.g., Jaremka et al., 2013; Gouin et al., 2009; Kiecolt-Glaser et al., 2005). A few studies have been based on undergraduate students who were closer in age as the present sample (e.g., Chiang et al., 2012; John-Henderson et al., 2015), but these studies assessed inflammation via oral fluids.

### **Psychosocial Functioning and HPA axis and sAA Responses to Stress (Secondary Aim)**

Theoretical models and prior empirical work suggest that psychosocial processes may drive HPA and SNS responses to stress (e.g., Luecken, 2006; Repetti, 2002). As such, we hypothesized that higher threat appraisals, greater emotional reactivity, and poorer social relationships would be related to heightened HPA and SNS responses to the TSST. In partial support of these hypotheses, we found that psychosocial processes were related to cortisol, but not sAA, responses. More specifically, greater emotional reactivity and more supportive relationships were related to higher levels of cortisol in response to the TSST whereas higher threat appraisals were related to dampened HPA activity.

The association between greater emotional reactivity and greater HPA responses to stress is in line with previous research showing that overall NA reactivity is related to greater cortisol reactivity. For instance, negative affect was associated with increases in cortisol in adolescents' everyday life (Doane & Zeiders, 2014). The current data further specify that fear and guilt reactivity to an acute stressor may be particularly important for HPA responses to stress. However, not all past studies on specific emotions of fear and guilt in relation to HPA function have demonstrated these links. Specifically, studies have shown both positive and negative associations between fear and cortisol responses (Lerner, Dahl, Hariri, & Taylor, 2007; Lupis, Lerman, & Wolf, 2014; Moons et al., 2010), and one past study on self-conscious emotions

indicated no relation between guilt and cortisol responses to a self-blame induction (Dickerson et al., 2004).

Contrary to the notion that positive aspects of social relationships attenuate cortisol responses to stress, we found that supportive relationships were related to enhanced cortisol reactivity to the TSST. At least a handful of past studies have found that aspects of social support (i.e., instrumental support, quantity of social support and overall social support) are associated with heightened cardiovascular reactivity to challenges (B. Hughes & Curtis, 2000; B. M. Hughes, 2005, 2007; Roy, Steptoe, & Kirschbaum, 1998; Schwerdtfeger & Schlagert, 2011; Tardy, Thompson, & Allen, 1989). Supported individuals may typically seek support to cope with stressors and may exhibit enhanced activation of the biological stress systems when encountering stress alone. Alternatively, given that activation of stress systems in the short-term is viewed as adaptive (McEwen, 1998), the relation between more supportive relationships and greater HPA activation in the present study could represent an adaptive and thus desirable response.

It is also possible that the inverse association between supportive relationships and HPA responses simply reflects the effect of early family stress on HPA axis functioning. In the present study, we found that a harsher family climate was related to dampened HPA responses to stress. The SPS assesses global perceptions of social support across relationships ties. Importantly, our sample consisted of late adolescents mostly from Latino backgrounds. The family is crucial for social support processes among Latinos (Campos & Shenhav, 2014) and remains a primary source of support for late adolescents (Galambos, Barker, & Almeida, 2003; Helsen, Vollebergh, & Meeus, 2000). To the extent that our measure of supportive relationships is primarily tapping into family relationships, it may be that the observed enhanced cortisol responses in relation to

more support reflects the link between lower early family stress and greater cortisol responses we observed in the present study.

The relation between higher threat appraisals and dampened cortisol responses was also unexpected given theoretical work on stress processes (Lazarus & Folkman, 1984). According to allostatic load theory (McEwen, 1998), repeated activation of biological stress systems can contribute to their dysregulation, resulting in blunted responses in the face of subsequent stress. Supporting this notion, chronic stress, fatigue, and burnout have been associated with hypocortisolism (Miller et al., 2007). Individuals who tend to appraise events and stimuli as more threatening may experience more frequent and/or repeated activation of the HPA axis. As mentioned above, over time, this can contribute to downregulation of the HPA axis. Thus, one possibility is that among those chronically stressed, high threat appraisals may be related to dampened cortisol reactivity. There was no evidence that the sample in the current study were chronically stressed. Future work is needed to clarify why higher threat appraisals may be related to dampened cortisol responses.

### **Gender, Ethnicity, and Subtypes of Early Family Stress (Exploratory Aims)**

**Gender and ethnicity.** The effects of early family stress on inflammatory, biobehavioral, and psychosocial processes did not vary by gender in the current study. Whereas some prior studies have demonstrated gender differences in the effects of early family stress (Bae et al., 2014; Godinet et al., 2014), others have not (Wickrama et al., 2008). Variation of the effects of early family stress by gender may occur under certain circumstances or for particular individuals. We currently do not understand when or why gender may modulate the effects of early family stress and more research is needed. The only gender difference we observed was in baseline levels of IL-6, with females showing greater baseline levels of IL-6 than males. This is consistent

with past epidemiological studies showing that adult women have higher levels of CRP than adult men (Khera et al., 2005; Lakoski et al., 2006).

We did find that ethnicity moderated some of the effects of early family stress. More specifically, the relations between early family stress and HPA activity, anger reactivity, and social relationships varied as a function of ethnicity. The relations between greater early family stress and dampened cortisol responses and poorer social relationships were only evident among Latinos and not among European Americans. By contrast, greater early family stress was related to decreased anger reactivity only among European-Americans, but not among those from Latino backgrounds. Why we observed these patterns of results remains unclear, but may have to do with the fact that salience of the family context and the extent to which certain family characteristics are valued varies between Latino and European Americans. A core belief of Latino heritage groups is familism, which is the view that the family constitutes the self and is the center of social relationships (Campos & Shenhav, 2014; Miranda, Bilot, Peluso, Berman, & Van Meek, 2006). Primary sources of support stem from the family, and emphasis is placed on harmonious family relationships, interconnectedness, and family obligations (Campos & Shenhav, 2014; Freeberg & Stein, 1996; Yee, DeBaryshe, Yuen, Kim, & McDubbin, 2007). Given these cultural views on family relationships, family-related stressors that disrupt family harmony and a lack of support may have particularly profound ramifications on the HPA axis, which is particularly sensitive to the environment during development (Gunnar & Donzella, 2002; Hostinar & Gunnar, 2013), and on social relationships among Latinos. Examination of cultural and ethnic differences in the effects of early adversity is limited, and thus future studies are needed to clarify these findings.

**Family stressor subtype.** We examined whether subtypes of stressors assessed by the Risky Families questionnaire was uniquely associated with particular biobehavioral and psychosocial variables. We found that independent of abuse and chaos, neglect was associated with blunted HPA, better sleep quality, greater reactivity of sadness, and lower levels of social support. Abuse was uniquely associated with poorer total sleep and greater dysfunction during day, and chaos was related to decreased NA reactivity and higher levels of SPS nurture. Together these findings suggest that subtypes of early family stressors have differential effects. The fact that we found differential effects is not entirely surprising given that the subtypes of stressors reflect different experiences. Abuse reflects threats and behavior directed at the individual, neglect involves depriving the individual from necessities or other positive behaviors, and chaos captures experiences occurring around the individual. Past studies have also found differential effects, though they are not entirely consistent with the present findings. For instance, studies have found that physical abuse is related to HPA reactivity (Kuhlman et al., 2015) and chaos is related to higher levels of inflammation (Crosswell et al., 2014). Therefore, the question of when, how, and why certain family stressors have effects on particular outcomes remains unanswered at this time.

### **Limitations and Future Directions**

Several limitations of the study should be noted. First, we relied on retrospective reports of early family stress. As such, they may have been subject to recall biases or influenced by affective states. However, the RF questionnaire has been shown to have high agreement with clinical interviews assessing early adversity and has been reliably linked to adverse mental and physical health outcomes (Taylor et al., 2004). Furthermore, the current sample was comprised of high school seniors and first-year college students, and many of them continued to live with

their families. This may have assisted in more accurate recall of their earlier family environment. Nevertheless, studies employing concurrent measures of early family adversity would likely provide a more precise picture of the effects of early family stress.

Second, the measure of early family stress used in the present study spans a broad window of time beginning in early childhood through mid-adolescence. Yet, the family social climate is known to change across time, especially from childhood to adolescence (Collins & Russell, 1991; Collins & Steinberg, 2006; Paikoff & Brooks-Gunn, 1991; Smetana, Campione-Barr, & Metzger, 2006; Tsai, Telzer, & Fuligni, 2013). Furthermore, biological systems and psychosocial functioning continue to develop from the neonatal period through adolescence, and adversity exposure during different periods of development may differentially impact these systems. Supporting this notion, one study demonstrated that adversities during prenatal and early postnatal periods, but not during late childhood and adolescence, were related to exaggerated cortisol responses to social stress during adolescence (N. M. Bosch et al., 2012). Another study focusing on inflammation showed that adversity during middle childhood, but not earlier adversity was related to higher levels of CRP at ages 10 and 15 (Slopen et al., 2013). The current study was not able to explore any timing effects given the measure of early family stress. Future research should examine whether early family stress during particular developmental stages have more profound or long-lasting effects on biological and psychosocial functioning that contribute to disease risk.

Third, the artificiality of the laboratory-controlled setting makes unclear whether the relations we observed in the present study would translate to naturalistic settings. Participants were in a clinic setting with several apparatuses attached to them, which does not reflect more typical stress experiences in everyday life. Moreover, many participants commented on the

ecological validity of the study, indicating that they suspected they were not truly being evaluated during the TSST and that the judges were actors. Thus, the contrived context may have contributed to findings. It would be beneficial for future research to employ daily diary methodology to address this concern and determine whether early adversity similarly influences biological and psychosocial responses to stress in everyday life to affect inflammation and physical health.

Fourth, the current study employed the TSST, which is just one type of social stressor. Features of stressors (e.g., severity, duration, social vs. non-social) may differentially affect biological stress systems and psychosocial responses. For instance, conflict with or rejection from important individuals may be more potent stressors for individuals experiencing early family stress given that early family stress can interfere with attachment in close relationships. It will be important for future work to clarify whether early family adversity similarly affects stress responsivity to all types of stressors.

Lastly, the long-term health consequences of the present findings are unknown. We did not observe any relation between early family stress and inflammation, but we found that early family stress was related to blunted HPA functioning, poorer sleep, higher threat appraisals and poorer social relationships. These factors are assumed to have implications for physical health outcomes. For instance, the detrimental effects on physical health of poor sleep have been well-documented (Gallicchio & Kalesan, 2009). Similarly, less social support has been shown to increase all cause-mortality (Berkman & Syme, 1979). However, because there was no inclusion of any physical health outcomes and the current sample was young and healthy, the health consequences of the effects of early family adversity on HPA axis, sleep, and psychosocial functioning cannot be ascertained in the present study. Thus, future work should include physical

health outcomes or clinically relevant markers of disease to determine with greater precision whether these are indeed viable pathways from early family stress to poor health.

## **Conclusion**

The present study examined how alterations in biological and psychosocial functioning associated with early family stress may lead to increased inflammatory activity. Results showed that late adolescents who experienced early family stress did not exhibit heightened inflammatory responses to an acute social stressor. The relation between early family stress and inflammatory processes may be complex during youth development and may only be evident when probing immune cells or in the context of severe stressors or vulnerability risk factors. Thus, more work is needed to ascertain when and how early family stress comes to affect inflammatory processes and ultimately health. There was evidence that individuals experiencing early family stress exhibit dampened cortisol activity, poor sleep, higher threat appraisals, and less supportive relationships. These results support several key tenets in theoretical models including the Risky Families Model (Repetti et al., 2002) and the Biological Embedding Model (Miller et al., 2011), which posit that early family-related stress leads to dysregulations of biological systems and psychosocial functioning to heighten inflammation and increase risk for chronic diseases. Longitudinal studies are needed in order to determine the physical health implications of these effects.

**Table 1.** *Descriptive Data of Study Variables*

|                                        | <i>Mean</i> | <i>SD</i> | <i>Min</i> | <i>Max</i> |
|----------------------------------------|-------------|-----------|------------|------------|
| <i>Sociodemographic Variables</i>      |             |           |            |            |
| Age                                    | 18.37       | .51       | 18.00      | 20.00      |
| Gender                                 | .57         | .50       | .00        | 1.00       |
| Ethnicity                              | .63         | .49       | .00        | 1.00       |
| Parent Education                       | 7.44        | 2.01      | 2.00       | 10.50      |
| <i>Potential Confounding Variables</i> |             |           |            |            |
| BMI                                    | 25.08       | 5.93      | 16.84      | 48.42      |
| Depressive symptoms (CESD)             | 13.38       | 9.69      | 0.00       | 42.00      |
| <i>Early Family Stress</i>             |             |           |            |            |
| Risky Families (RF) Total Score        | 1.92        | .60       | 1.00       | 3.92       |
| RF Abuse                               | 1.72        | .79       | 1.00       | 4.50       |
| RF Neglect                             | 1.53        | .89       | 1.00       | 4.50       |
| RF Chaos                               | 1.70        | .70       | 1.00       | 4.25       |
| <i>Inflammation</i>                    |             |           |            |            |
| Baseline IL-6                          | 1.47        | 1.39      | .34        | 7.53       |
| IL-6 Reactivity (change score)         | .50         | .99       | -1.39      | 7.47       |
| <i>HPA Axis Variables</i>              |             |           |            |            |
| Baseline Cortisol                      | 16.84       | 15.69     | 3.51       | 111.16     |
| Cortisol AUCg                          | 1518.79     | 897.61    | 403.92     | 6756.66    |
| Cortisol AUCi                          | 131.96      | 847.86    | -2899.39   | 2431.30    |
| Cortisol reactivity (change score)     | 7.76        | 15.88     | -39.76     | 54.67      |
| Cortisol recovery (change score)       | -10.40      | 11.51     | -48.61     | 23.71      |
| <i>SNS Variables</i>                   |             |           |            |            |
| Baseline sAA                           | 88.67       | 102.79    | 5.19       | 762.43     |
| sAA AUCg                               | 8298.08     | 5776.41   | 748.59     | 30591.29   |
| sAA AUCi                               | 1979.01     | 3041.65   | -4172.86   | 12157.84   |
| sAA reactivity (change score)          | 61.46       | 86.63     | -219.89    | 352.08     |
| sAA recovery (change score)            | -21.48      | 62.41     | -339.60    | 96.60      |
| <i>Sleep Variables</i>                 |             |           |            |            |
| Sleep diary latency (hours)            | .29         | .28       | .03        | 1.78       |
| Sleep diary duration (hours)           | 8.14        | 1.24      | 4.14       | 11.08      |
| Sleep diary efficiency                 | .96         | .03       | .86        | 1.00       |
| PSQI sleep duration                    | .27         | .56       | .00        | 3.00       |

|                                                |      |      |       |       |
|------------------------------------------------|------|------|-------|-------|
| PSQI Disturbance                               | 1.13 | .52  | .00   | 2.00  |
| PSQI latency                                   | .86  | .86  | .00   | 3.00  |
| PSQI day dysfunction                           | .93  | .77  | .00   | 3.00  |
| PSQI efficiency                                | .48  | .83  | .00   | 3.00  |
| PSQI quality                                   | .88  | .56  | .00   | 2.00  |
| PSQI total                                     | 4.79 | 2.42 | .00   | 12.00 |
| <i>Cognitive Appraisal Variables</i>           |      |      |       |       |
| Anticipatory threat appraisal                  | .86  | .26  | .44   | 1.74  |
| Retrospective threat appraisal                 | 1.21 | .62  | .52   | 3.75  |
| <i>Emotional Reactivity Variables</i>          |      |      |       |       |
| NA reactivity                                  | .44  | .64  | -.88  | 3.50  |
| Fear reactivity                                | .41  | .84  | -1.80 | 3.20  |
| Anger reactivity                               | .46  | .70  | -.50  | 3.00  |
| Guilt reactivity                               | .53  | .87  | -.60  | 3.80  |
| Sad reactivity                                 | .15  | .58  | -1.33 | 3.00  |
| <i>Supportive Relationship Variables (SPS)</i> |      |      |       |       |
| Supportive relationships                       | 3.37 | .37  | 2.04  | 3.96  |
| Emotional closeness                            | 3.40 | .54  | 1.75  | 4.00  |
| Integration                                    | 3.45 | .56  | 1.00  | 4.00  |
| Reassurance of worth                           | 3.20 | .49  | 2.00  | 4.00  |
| Tangible support                               | 3.63 | .43  | 2.50  | 4.00  |
| Informational support                          | 3.66 | .50  | 1.75  | 4.00  |
| Nurturance                                     | 2.91 | .59  | 1.25  | 4.00  |

*Note.* Categories for parent education were 1=some elementary school, 2 =completed elementary school, 3=some junior high school, 4=completed junior high school, 5=some high school, 6=graduated high school, 7=trade or vocational school, 8=some college, 9=graduated from college, 10=some medical, law, or graduate school, and 11 = graduated from medical, law, or graduate school. Inflammatory, HPA axis, and SNS variables are presented in raw values. Inflammatory reactivity = 90 minute post TSST – baseline. Cortisol reactivity = 30 minute post TSST – baseline. Cortisol recovery = 75 minute post TSST – 30 minute post TSST. sAA reactivity = post TSST – baseline. sAA recovery = post TSST – 75 minute post TSST. BMI =

body mass index. CESD = Center for Epidemiologic Studies Depression Scale. AUC = area under the curve. sAA = salivary alpha-amylase. SPS = Social Provisions Scale.

**Table 2a.** *Bivariate Correlations between Early Family Stress, Inflammatory Reactivity, and Control Variables.*

| Variable                             | 1 | 2     | 3     | 4     | 5   | 6   | 7    | 8     | 9      | 10    | 11    |
|--------------------------------------|---|-------|-------|-------|-----|-----|------|-------|--------|-------|-------|
| 1. RF                                |   | .81** | .74** | .81** | .05 | .14 | -.08 | .25*  | -.13   | .18   | .45** |
| 2. RF abuse                          |   |       | .59** | .51** | .04 | .01 | -.17 | .19   | .01    | .09   | .32** |
| 3. RF neglect                        |   |       |       | .49** | .05 | .17 | -.16 | .29** | -.19   | .11   | .31** |
| 4. RF chaos                          |   |       |       |       | .05 | .12 | -.02 | .30** | -.17   | .21   | .35** |
| 5. IL-6 Reactivity<br>(change score) |   |       |       |       |     | .18 | .14  | -.10  | -.08   | -.03  | .17   |
| 6. Age                               |   |       |       |       |     |     | .09  | .10   | -.29** | .17   | .11   |
| 7. Gender                            |   |       |       |       |     |     |      | -.07  | -.08   | .09   | -.01  |
| 8. Ethnicity                         |   |       |       |       |     |     |      |       | -.41** | .15   | -.01  |
| 9. Parent Education                  |   |       |       |       |     |     |      |       |        | -.24* | -.04  |
| 10. BMI                              |   |       |       |       |     |     |      |       |        |       | -.04  |
| 11. Depressive<br>symptoms           |   |       |       |       |     |     |      |       |        |       |       |

$p < .05$ ; \*\*  $p < .01$ ; \*\*\*  $p < .001$ .

**Table 2b.** *Bivariate Correlations between Early Family Stress, Inflammatory Reactivity, Control, and HPA and SNS Variables.*

| Variable                                    | RF     | RF<br>abuse | RF<br>neglect | RF<br>chaos | ln IL6<br>reactivity<br>(change<br>score) | Age  | Gender | Ethnicity | Parent<br>Education | BMI  | Depressive<br>symptoms |
|---------------------------------------------|--------|-------------|---------------|-------------|-------------------------------------------|------|--------|-----------|---------------------|------|------------------------|
| Cortisol<br>AUCg                            | -.29** | -.28**      | -.19          | -.25*       | -.21                                      | -.08 | -.17   | .00       | .08                 | -.01 | -.13                   |
| Cortisol<br>AUCi                            | -.15   | -.11        | -.20          | -.08        | .13                                       | -.06 | .12    | .13       | -.19                | .14  | .12                    |
| Cortisol<br>Reactivity<br>(change<br>score) | -.14   | -.15        | -.22*         | -.06        | .05                                       | -.08 | .09    | .22*      | -.24*               | .17  | .12                    |
| Cortisol<br>Recovery<br>(change<br>score)   | .13    | .26*        | .22*          | .02         | .15                                       | .08  | -.01   | -.27*     | .13                 | -.13 | .01                    |
| sAA AUCg                                    | -.08   | .02         | -.03          | -.14        | -.12                                      | .03  | -.09   | .04       | .06                 | .18  | -.18                   |
| sAA AUCi                                    | .06    | .00         | .04           | .08         | .00                                       | -.02 | -.13   | -.20      | .00                 | -.09 | .15                    |
| sAA<br>Reactivity<br>(change<br>score)      | .01    | -.08        | -.04          | .06         | .05                                       | -.07 | -.01   | -.29**    | .03                 | .03  | .03                    |
| sAA<br>Recovery                             | -.07   | -.07        | .09           | -.07        | -.18                                      | -.05 | -.02   | .15       | -.05                | .05  | .03                    |

$p < .05$ ; \*\*  $p < .01$ ; \*\*\*  $p < .001$ .

**Table 2c.** *Bivariate Correlations between Early Family Stress, Inflammatory Reactivity, Control, and Sleep Variables.*

| Variable                           | RF    | RF<br>abuse | RF<br>neglect | RF<br>chaos | ln IL6<br>reactivity<br>(change<br>score) | Age   | Gender | Ethnicity | Parent<br>Education | BMI  | Depressive<br>symptoms |
|------------------------------------|-------|-------------|---------------|-------------|-------------------------------------------|-------|--------|-----------|---------------------|------|------------------------|
| Sleep Diary<br>Latency<br>(hours)  | .04   | .00         | .11           | -.05        | .11                                       | .33** | .10    | .06       | -.15                | .03  | .18                    |
| Sleep Diary<br>Duration<br>(hours) | -.01  | -.02        | -.04          | -.04        | -.05                                      | .14   | .21*   | .09       | -.12                | .14  | -.16                   |
| Sleep Diary<br>Efficiency          | -.02  | -.01        | -.08          | .05         | -.16                                      | -.26* | -.10   | -.03      | .04                 | .00  | -.19                   |
| PSQI Sleep<br>Duration             | .02   | -.02        | -.06          | .10         | .02                                       | -.06  | .05    | .09       | -.06                | .13  | .06                    |
| PSQI<br>Disturbance                | .20   | .20         | .08           | .21*        | .04                                       | -.02  | .01    | -.11      | .01                 | -.01 | .28**                  |
| PSQI<br>Latency                    | .20   | .22*        | .18           | .07         | .16                                       | .17   | .14    | .00       | -.05                | .11  | .30**                  |
| PSQI Day<br>Dysfunction            | .32** | .41**       | .17           | .19         | .16                                       | .14   | -.05   | -.19      | .25*                | -.20 | .38**                  |
| PSQI<br>Efficiency                 | -.07  | -.07        | -.13          | .02         | -.08                                      | -.04  | .13    | .09       | .02                 | .14  | -.07                   |
| PSQI<br>Quality                    | .17   | .16         | -.01          | .21         | .00                                       | .09   | .01    | .04       | -.20                | .06  | .27**                  |
| PSQI Total                         | .21*  | .25*        | .07           | .18         | .13                                       | .04   | .11    | -.05      | -.03                | .08  | .31**                  |

$p < .05$ ; \*\*  $p < .01$ ; \*\*\*  $p < .001$ .

**Table 2d.** *Bivariate Correlations between Early Family Stress, Inflammatory Reactivity, Control, and Psychosocial variables.*

|                                       | RF     | RF<br>abuse | RF<br>neglect | RF<br>chaos | ln IL6<br>reactivity<br>(change<br>score) | Age  | Gender | Ethnicity | Parent<br>Education | BMI   | Depressi<br>ve<br>symptom<br>s |
|---------------------------------------|--------|-------------|---------------|-------------|-------------------------------------------|------|--------|-----------|---------------------|-------|--------------------------------|
| Anticipatory<br>threat<br>appraisal   | .22*   | .21         | .22*          | .09         | -.01                                      | -.16 | .00    | .11       | .19                 | -.10  | .04                            |
| Retrospectiv<br>e threat<br>appraisal | .34**  | .31**       | .30**         | .20         | .07                                       | -.01 | .05    | -.07      | .18                 | -.07  | .35**                          |
| NA<br>reactivity                      | -.06   | -.11        | .03           | -.13        | .15                                       | .01  | -.01   | -.12      | -.12                | -.15  | .38**                          |
| Fear<br>reactivity                    | .07    | -.04        | .15           | -.01        | .17                                       | -.04 | .10    | .08       | -.21                | .02   | .28**                          |
| Anger<br>reactivity                   | -.12   | -.10        | -.03          | -.13        | .02                                       | .05  | .04    | -.20      | .01                 | -.23* | .30**                          |
| Guilt<br>reactivity                   | -.11   | -.09        | .03           | -.22*       | -.01                                      | -.15 | -.08   | -.06      | -.00                | -.18  | .30**                          |
| Sad<br>reactivity                     | .09    | .04         | .24*          | -.03        | -.03                                      | -.07 | -.10   | .07       | .01                 | .02   | .15                            |
| Supportive<br>relationships<br>(SPS)  | -.39** | -.33**      | -.37**        | -.28**      | -.10                                      | .19  | .20    | -.06      | -.17                | .11   | -.38**                         |
| SPS<br>emotional<br>closeness         | -.33** | -.29**      | -.20*         | -.22*       | -.02                                      | .18  | .32**  | -.09      | -.06                | .07   | -.33**                         |

|                           |        |        |        |        |      |      |       |      |       |     |        |
|---------------------------|--------|--------|--------|--------|------|------|-------|------|-------|-----|--------|
| SPS integration           | -.25*  | -.16   | -.17   | -.22*  | -.03 | .14  | -.12  | .05  | -.15  | .05 | -.38** |
| SPS reassurance of worth  | -.48** | -.45** | -.37** | -.41** | -.11 | -.06 | .13   | -.14 | -.07  | .01 | -.34** |
| SPS tangible support      | -.41** | -.38** | -.52** | -.28** | -.13 | .21  | .30** | -.06 | -.07  | .10 | -.29** |
| SPS informational support | -.30** | -.18   | -.31** | -.30** | -.08 | .16  | .07   | -.05 | -.11  | .09 | -.29** |
| SPS nurturance            | .03    | -.04   | -.06   | .17    | -.08 | .17  | .17   | .02  | -.24* | .14 | -.02   |

$p < .05$ ; \*\*  $p < .01$ ; \*\*\*  $p < .001$ .

**Table 3.** *Multilevel Growth Curve Model Predicting IL-6 from Early Family Stress x Time*

|                              | <i>b</i> | <i>SE</i> |
|------------------------------|----------|-----------|
| Intercept                    | -.34     | .11**     |
| Age                          | .03      | .10       |
| Gender                       | .54      | .10***    |
| Ethnicity                    | .21      | .11       |
| Parent Education             | -.01     | .03       |
| BMI                          | .06      | .01***    |
| Time                         | .01      | .03       |
| Time x Time                  | .04      | .01       |
| Risky Families               | -.12     | .10       |
| Time x Risky Families        | -.04     | .05       |
| Time x Time x Risky Families | .01      | .01       |

*Note.* All variables except gender and ethnicity were grand-mean centered. Gender was coded as 0 = male, 1 = female. Ethnicity was coded as 0 = European American, 1 = Latino.

$p < .05$ ; \*\*  $p < .01$ ; \*\*\*  $p < .001$ .

**Table 4.** *Multilevel Growth Curve Model Predicting Cortisol from Early Family Stress x Time*

|                              | <i>b</i> | <i>SE</i> |
|------------------------------|----------|-----------|
| Intercept                    | 2.65     | .11***    |
| Age                          | -.01     | .10       |
| Gender                       | -.17     | .10       |
| Ethnicity                    | .05      | .11       |
| Parent Education             | .01      | .03       |
| Time                         | .27      | .03***    |
| Time x Time                  | -.06     | .01***    |
| Risky Families               | -.17     | .11       |
| Time x Risky Families        | -.12     | .05**     |
| Time x Time x Risky Families | .02      | .01**     |

*Note.* All variables except gender and ethnicity were grand-mean centered. Gender was coded as 0 = male, 1 = female. Ethnicity was coded as 0 = European American, 1 = Latino.

\*  $p \leq .05$ ; \*\*  $p \leq .01$ ; \*\*\*  $p \leq .001$ .

**Table 5.** *Multilevel Growth Curve Model Predicting IL-6 from Cortisol AUCi x Time*

|                                | <i>b</i> | <i>SE</i>          |
|--------------------------------|----------|--------------------|
| Intercept                      | -1.70    | .24***             |
| Age                            | .04      | .10                |
| Gender                         | .53      | .10***             |
| Ethnicity                      | .15      | .11                |
| Parent Education               | .00      | .03                |
| BMI                            | .06      | .01***             |
| Time                           | .01      | .03                |
| Time x Time                    | .04      | .01***             |
| ln Cortisol AUCi               | .001     | .001               |
| Time x ln Cortisol AUCi        | .002     | .001*              |
| Time x Time x ln Cortisol AUCi | .0004    | .0002 <sup>a</sup> |

*Note.* All variables except gender and ethnicity were grand-mean centered. Gender was coded as 0 = male, 1 = female. Ethnicity was coded as 0 = European American, 1 = Latino.

\*  $p \leq .05$ ; \*\*  $p \leq .01$ ; \*\*\*  $p \leq .001$ .

**Table 6.** *Multilevel Growth Curve Model Predicting sAA from Early Family Stress x Time*

|                              | <i>b</i> | <i>SE</i> |
|------------------------------|----------|-----------|
| Intercept                    | 4.18     | .18***    |
| Age                          | .24      | .16       |
| Gender                       | -.10     | .16       |
| Ethnicity                    | .17      | .18       |
| Parent Education             | .03      | .04       |
| Time                         | .17      | .04***    |
| Time x Time                  | -.04     | .01***    |
| Risky Families               | -.24     | .16       |
| Time x Risky Families        | .08      | .06       |
| Time x Time x Risky Families | -.02     | .01       |

*Note.* All variables except gender and ethnicity were grand-mean centered. Gender was coded as 0 = male, 1 = female. Ethnicity was coded as 0 = European American, 1 = Latino.

\*  $p \leq .05$ ; \*\*  $p \leq .01$ ; \*\*\*  $p \leq .001$ .

**Table 7.** *Multiple Regression Models Predicting PSQI Sleep Variables from Early Family Stress.*

|                  | PSQI Total |           | PSQI Duration |           | PSQI Disturbance |           | PSQI Latency |                  | PSQI Day Dysfunction |                  | PSQI Efficiency |           | PSQI Quality |           |
|------------------|------------|-----------|---------------|-----------|------------------|-----------|--------------|------------------|----------------------|------------------|-----------------|-----------|--------------|-----------|
|                  | <i>b</i>   | <i>SE</i> | <i>b</i>      | <i>SE</i> | <i>b</i>         | <i>SE</i> | <i>b</i>     | <i>SE</i>        | <i>b</i>             | <i>SE</i>        | <i>b</i>        | <i>SE</i> | <i>b</i>     | <i>SE</i> |
| Intercept        | 3.93       | 10.16     | 2.30          | 2.66      | 1.86             | 2.19      | -4.16        | 3.61             | 3.27                 | 2.99             | 1.65            | 4.07      | .35          | 2.31      |
| Risky Families   | 1.01       | .45*      | .01           | .11       | .21              | .10*      | .29          | .16 <sup>a</sup> | .54                  | .14***           | -.12            | .16       | .16          | .10       |
| Age              | -.04       | .54       | -.11          | .14       | -.05             | .12       | .24          | .19              | -.20                 | .16              | -.07            | .21       | .03          | .12       |
| Gender           | .62        | .53       | .07           | .13       | .01              | .11       | .25          | .19              | -.03                 | .16              | .22             | .19       | -.01         | .12       |
| Ethnicity        | -.54       | .60       | .07           | .14       | -.21             | .13       | -.07         | .21              | -.34                 | .18 <sup>a</sup> | .21             | .22       | -.05         | .14       |
| Parent Education | -.05       | .15       | -.02          | .04       | -.01             | .03       | .00          | .05              | .06                  | .04              | .02             | .06       | -.05         | .03       |

*Note.* All variables except gender and ethnicity were grand-mean centered. Gender was coded as 0 = male, 1 = female. Ethnicity was coded as 0 = European American, 1 = Latino.

\*  $p \leq .05$ ; \*\*  $p \leq .01$ ; \*\*\*  $p \leq .001$  <sup>a</sup> marginal  $p = .07$ .

**Table 8.** *Multiple Regression Models Predicting Threat Appraisals from Early Family Stress.*

|                  | Anticipatory Threat Appraisals |           | Retrospective Threat Appraisals |           |
|------------------|--------------------------------|-----------|---------------------------------|-----------|
|                  | <i>b</i>                       | <i>SE</i> | <i>b</i>                        | <i>SE</i> |
| Intercept        | 1.78                           | 1.07      | .30                             | 2.45      |
| Risky Families   | .11                            | .05*      | .41                             | .11***    |
| Age              | -.08                           | .06       | -.02                            | .13       |
| Gender           | .04                            | .06       | .12                             | .13       |
| Ethnicity        | .10                            | .06       | -.11                            | .14       |
| Parent Education | .03                            | .02*      | .06                             | .04       |

*Note.* Gender was coded as 0 = male, 1 = female. Ethnicity was coded as 0 = European American, 1 = Latino.

\*  $p \leq .05$ ; \*\*  $p \leq .01$ ; \*\*\*  $p \leq .001$ .

**Table 9.** *Multiple Regression Models Predicting Emotional Reactivity from Early Family Stress.*

|                  | NA Reactivity |           | Fear Reactivity |           | Anger Reactivity |           | Guilt Reactivity |           | Sad Reactivity |           |
|------------------|---------------|-----------|-----------------|-----------|------------------|-----------|------------------|-----------|----------------|-----------|
|                  | <i>b</i>      | <i>SE</i> | <i>b</i>        | <i>SE</i> | <i>b</i>         | <i>SE</i> | <i>b</i>         | <i>SE</i> | <i>b</i>       | <i>SE</i> |
| Intercept        | 1.25          | 2.58      | 4.03            | 3.53      | -.87             | 2.94      | 5.22             | 3.47      | 1.31           | 2.47      |
| Risky Families   | -.03          | .11       | .09             | .16       | -.10             | .13       | -.12             | .15       | .08            | .11       |
| Age              | -.01          | .14       | -.18            | .19       | .10              | .16       | -.22             | .18       | -.08           | .13       |
| Gender           | -.04          | .13       | .16             | .18       | -.01             | .15       | -.14             | .18       | -.08           | .13       |
| Ethnicity        | -.18          | .15       | .04             | .21       | -.27             | .17       | .00              | .20       | .10            | .15       |
| Parent Education | -.06          | .04       | -.09            | .05       | -.02             | .04       | -.04             | .05       | .01            | .04       |

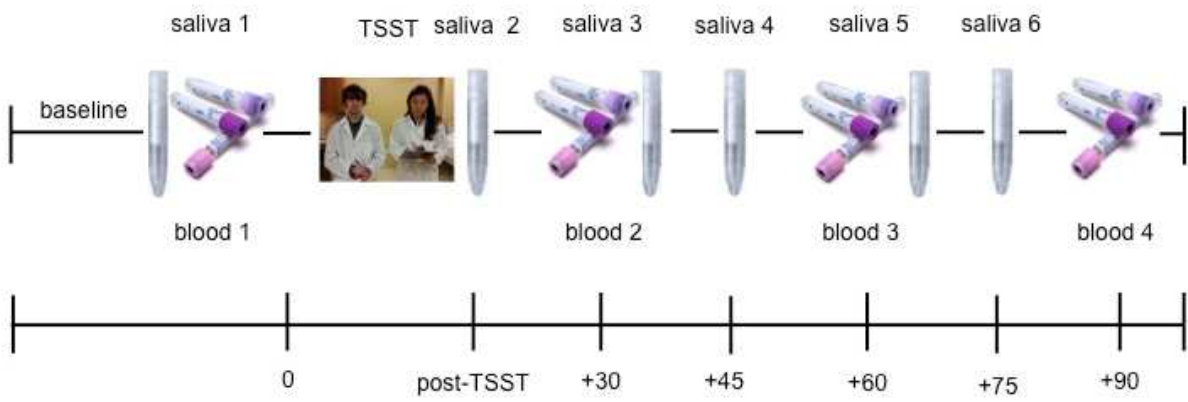
*Note.* Gender was coded as 0 = male, 1 = female. Ethnicity was coded as 0 = European American, 1 = Latino.

**Table 10.** *Multiple Regression Models Predicting Supportive Relationships from Early Family Stress.*

|                  | SPS      |           | Emotional Closeness |           | Integration |           | Reassurance of Worth |           | Tangible Support |           | Informational Support |           | Nurturance |           |
|------------------|----------|-----------|---------------------|-----------|-------------|-----------|----------------------|-----------|------------------|-----------|-----------------------|-----------|------------|-----------|
|                  | <i>b</i> | <i>SE</i> | <i>b</i>            | <i>SE</i> | <i>b</i>    | <i>SE</i> | <i>b</i>             | <i>SE</i> | <i>b</i>         | <i>SE</i> | <i>b</i>              | <i>SE</i> | <i>b</i>   | <i>SE</i> |
| Intercept        | 1.48     | 1.35      | -.08                | 2.02      | 1.03        | 2.24      | 4.84                 | 1.79**    | .50              | 1.54      | 1.11                  | 2.02      | 1.47       | 2.36      |
| Risky Families   | -.25     | .06***    | -.30                | .09***    | -.30        | .10**     | -.38                 | .08***    | -.30             | .07***    | -.27                  | .09**     | .03        | .10       |
| Age              | .14      | .07*      | .21                 | .11*      | .18         | .12       | -.03                 | .09       | .20              | .08*      | .18                   | .11       | .10        | .12       |
| Gender           | .10      | .07       | .30                 | .10**     | -.20        | .12       | .07                  | .09       | .22              | .08*      | .02                   | .10       | .20        | .12       |
| Ethnicity        | .00      | .08       | .02                 | .12       | .07         | .13       | -.05                 | .11       | .05              | .09       | -.02                  | .12       | -.06       | .14*      |
| Parent Education | -.03     | .02       | -.01                | .03       | -.04        | .03       | -.04                 | .03       | -.01             | .02       | -.03                  | .03       | -.07       | .03       |

*Note.* Gender was coded as 0 = male, 1 = female. Ethnicity was coded as 0 = European American, 1 = Latino.

\*  $p \leq .05$ ; \*\*  $p \leq .01$ ; \*\*\*  $p \leq .001$ .



*Figure 1.* Experimental session timeline.

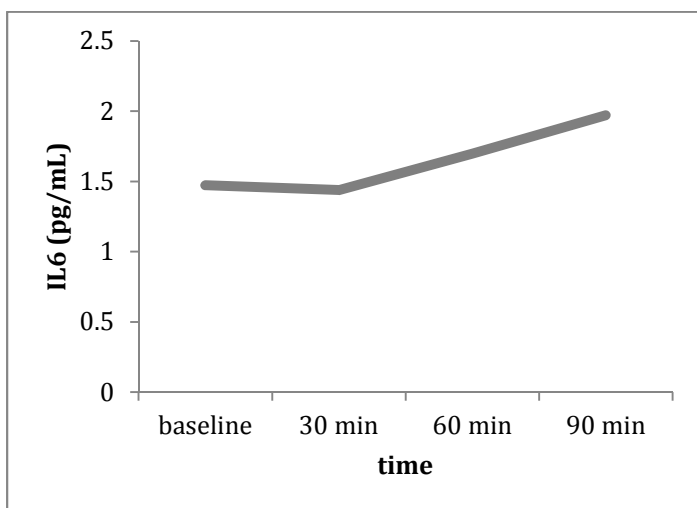


Figure 2a. IL-6 increased from 30 minutes to 90 minutes post-TSST across the study sample.

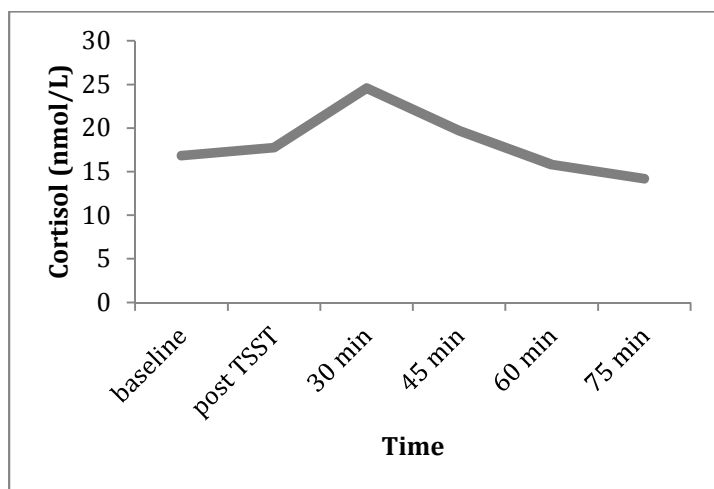


Figure 2b. Cortisol peaked 30 minutes post-TSST across the study sample.

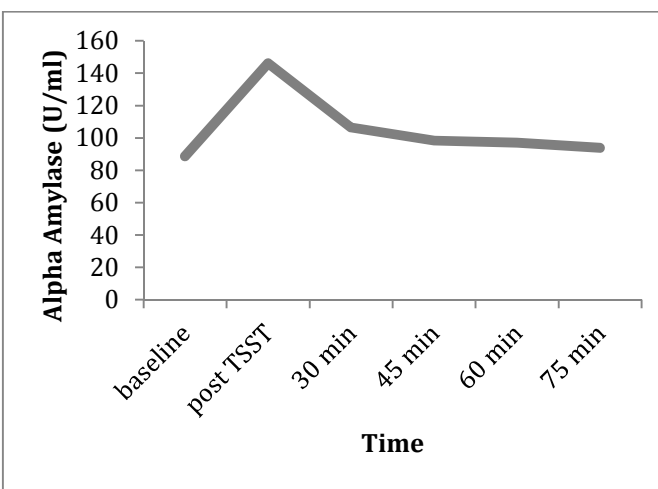
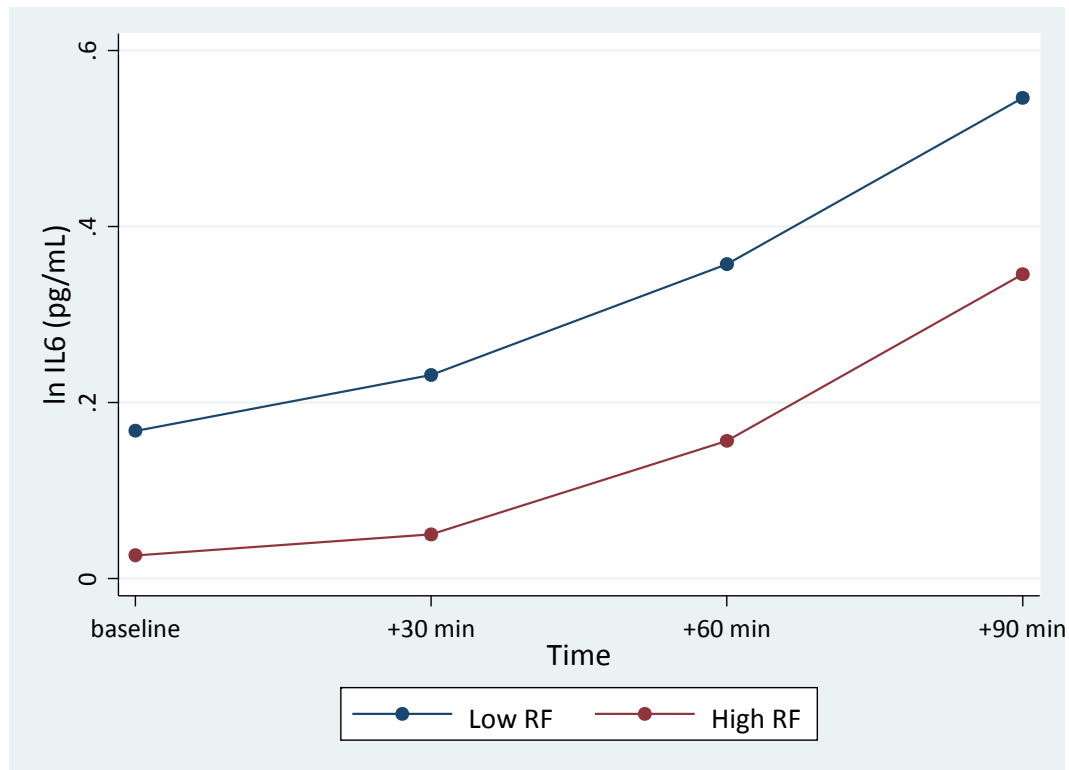
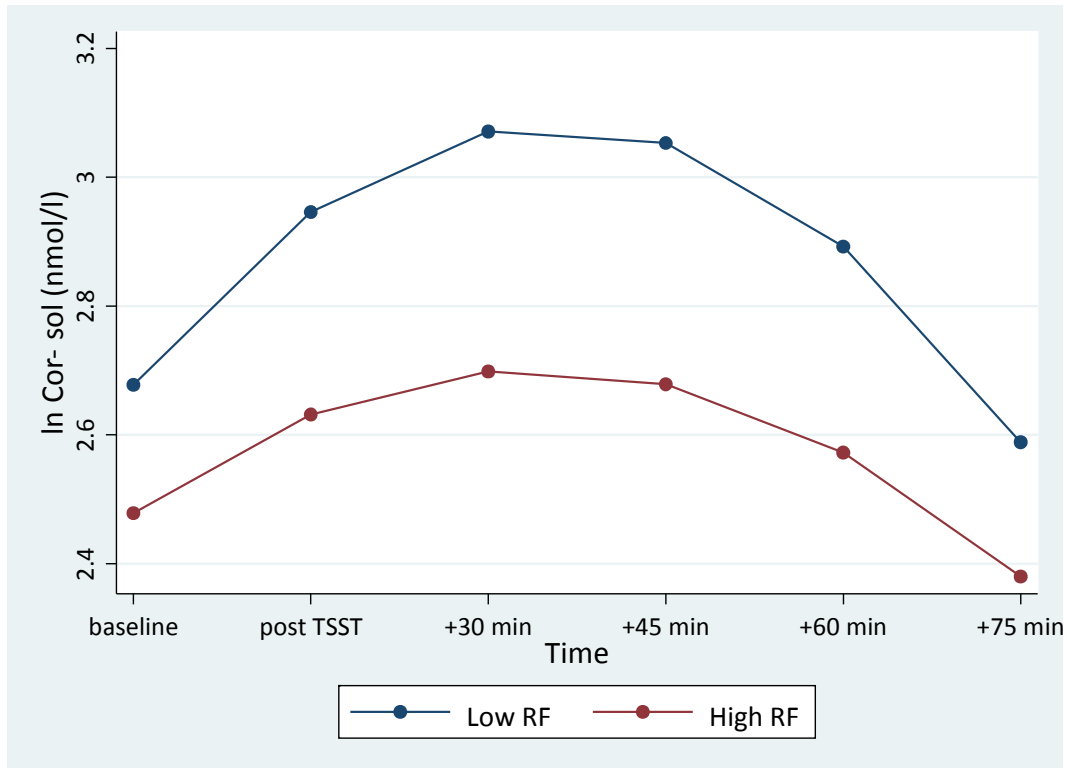


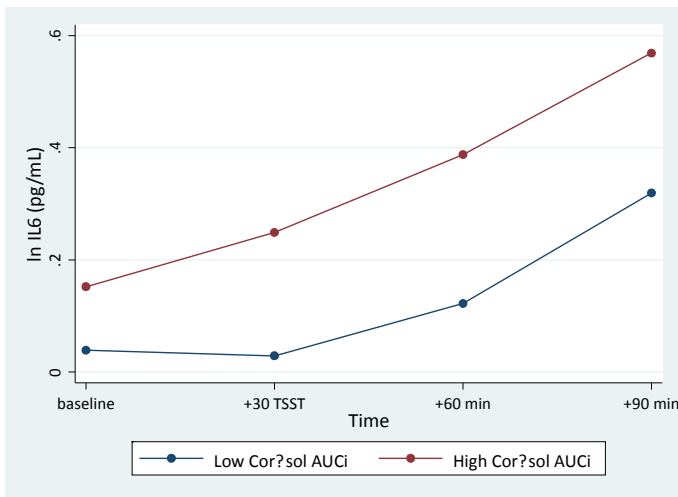
Figure 2c. sAA peaked 30 minutes post-TSST across the study sample.



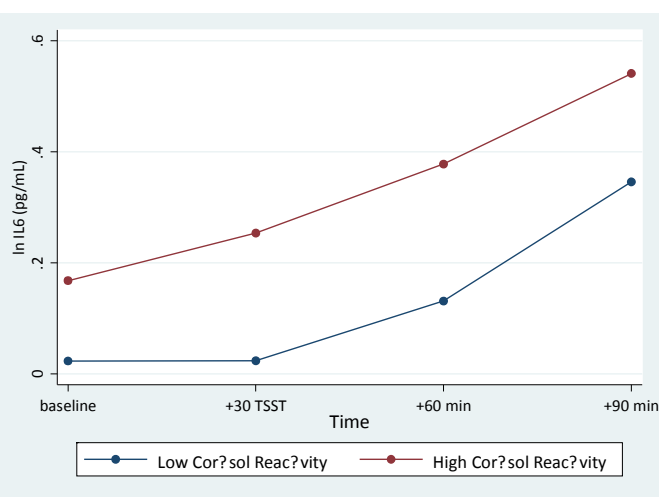
*Figure 3.* IL-6 slopes did not differ between individuals who experienced low levels of early family stress and those who experienced high levels of early family stress.



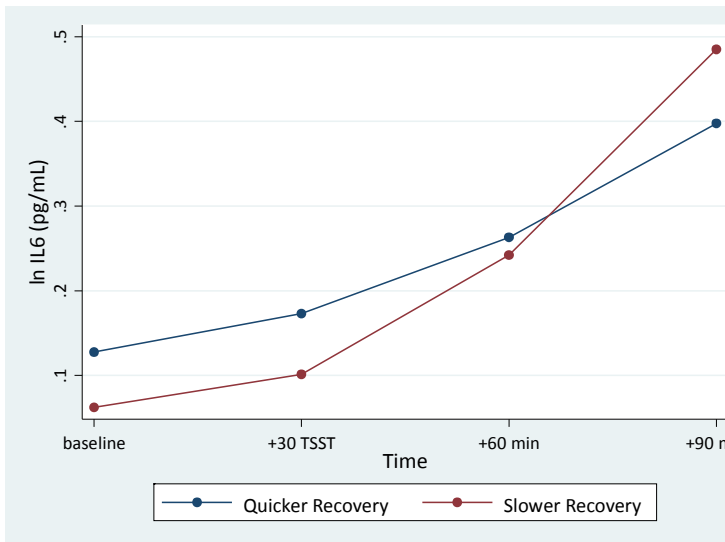
*Figure 4.* Individuals who experienced high levels of early family stress exhibited dampened cortisol responses to the TSST.



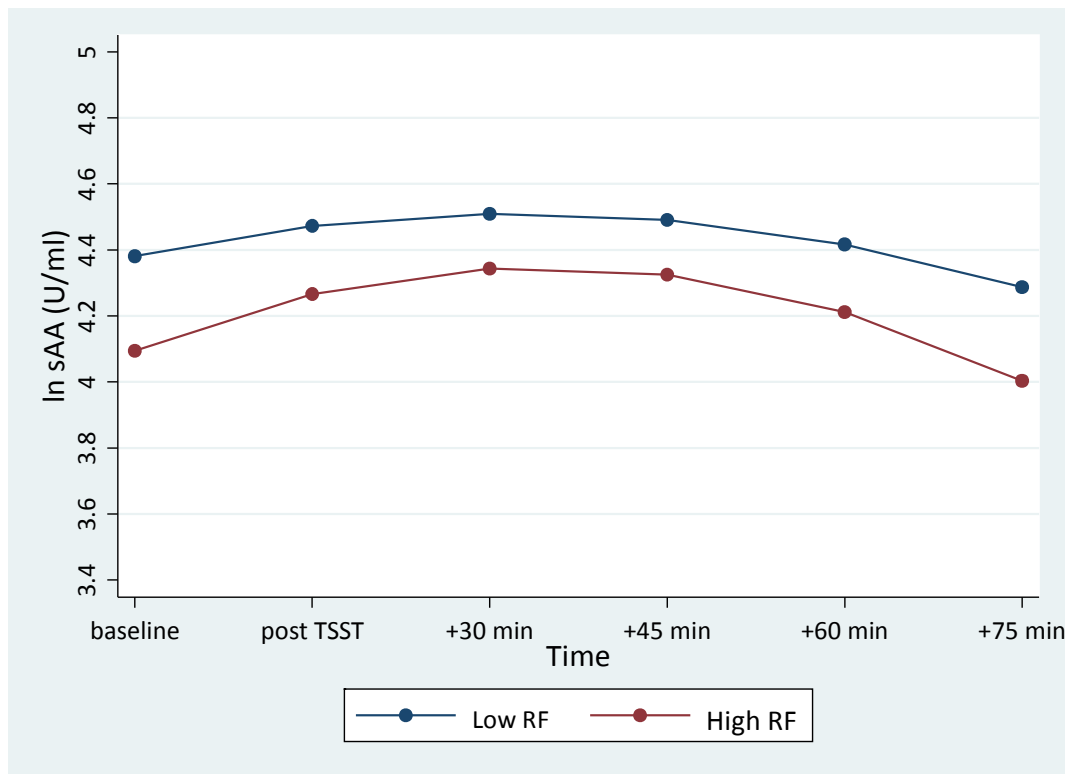
*Figure 5a.* There was an accelerated increase in IL-6 for individuals with higher cortisol AUCi.



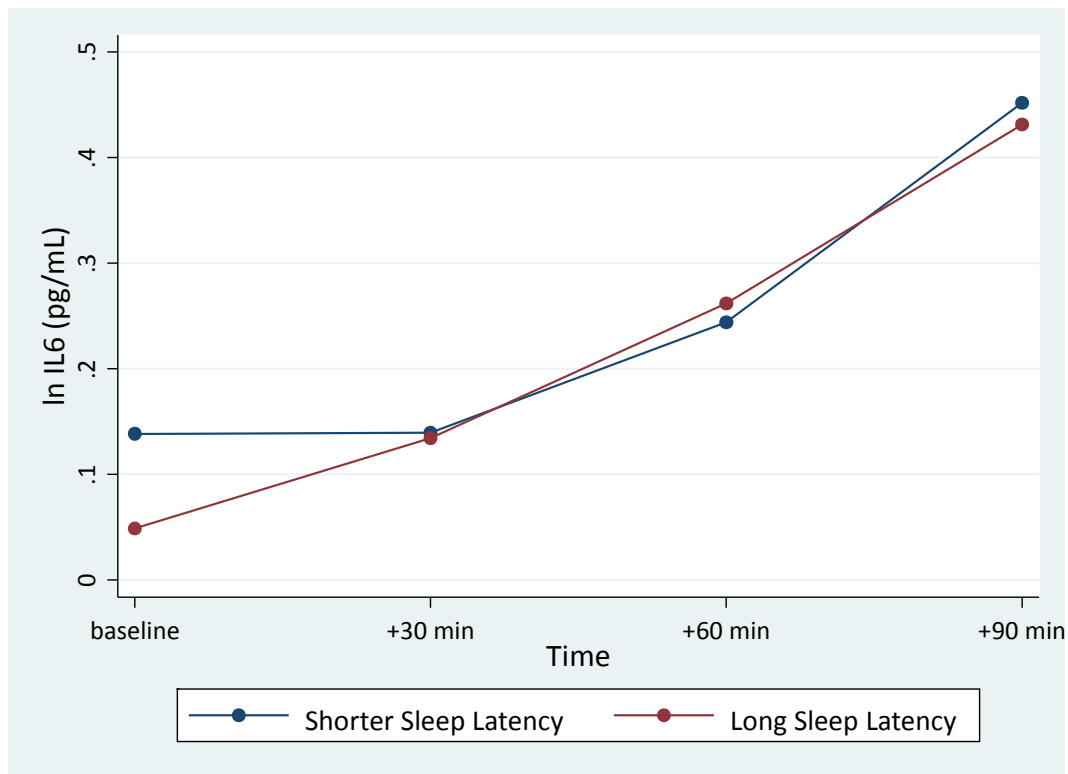
*Figure 5b* There was an accelerated increase in IL-6 for individuals with higher cortisol reactivity (change scores).



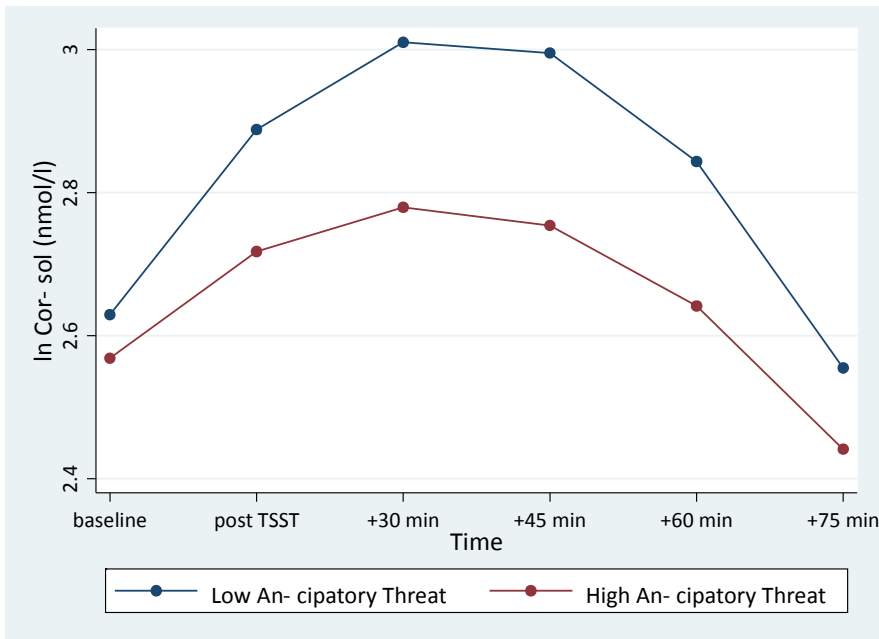
*Figure 5c.* There was an accelerated increase in IL-6 for individuals with slower recovery.



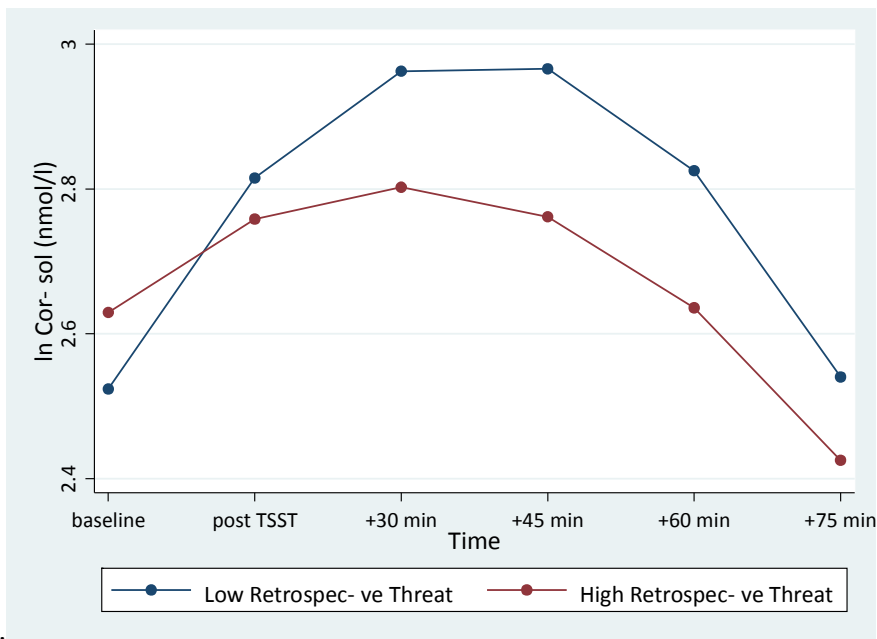
*Figure 6.* sAA responses to the TSST did not differ between individuals of high and low levels of early family stress.



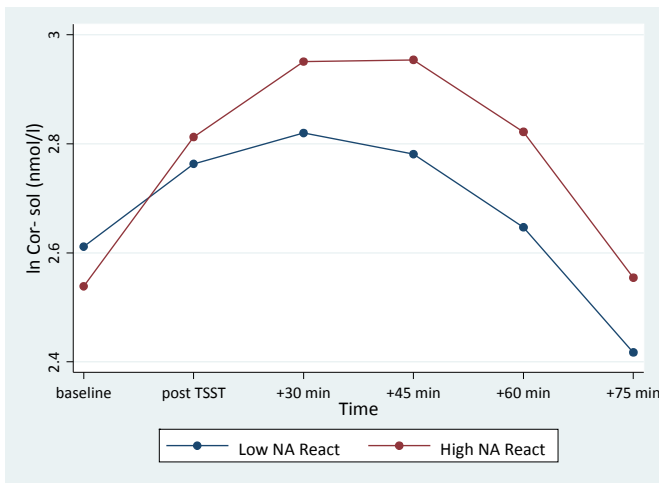
*Figure 7.* There was an accelerated increase in IL-6 for individuals with shorter sleep latency, but the change in slopes was due to higher levels of baseline IL-6.



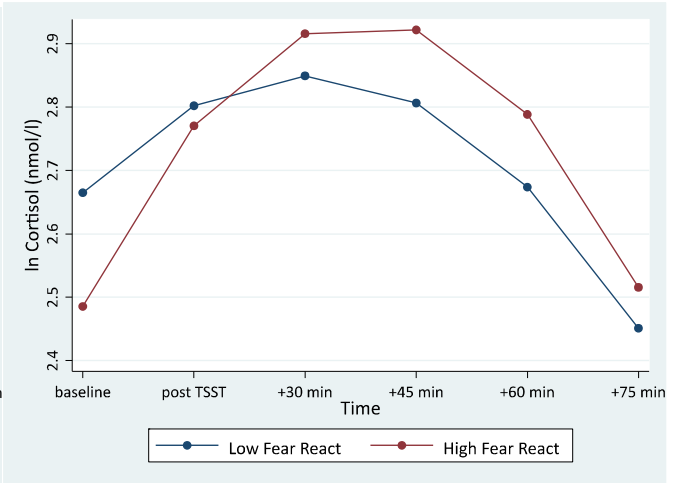
*Figure 8a.* Cortisol responses were attenuated for individuals with higher anticipatory threat appraisals compared to those with lower anticipatory threat appraisals.



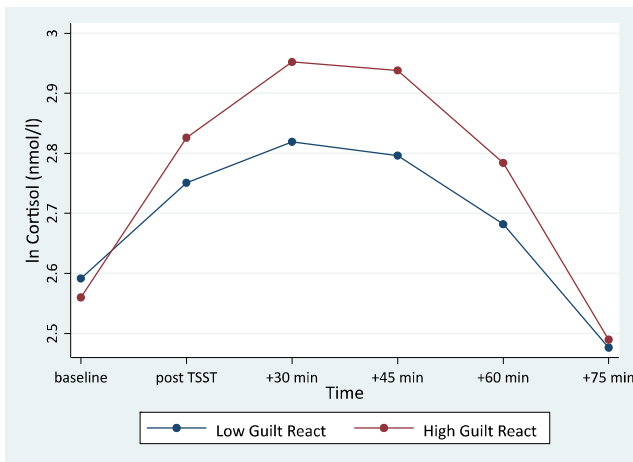
*Figure 8b.* Cortisol responses were attenuated for individuals with higher retrospective threat appraisals compared to those with lower retrospective threat appraisals.



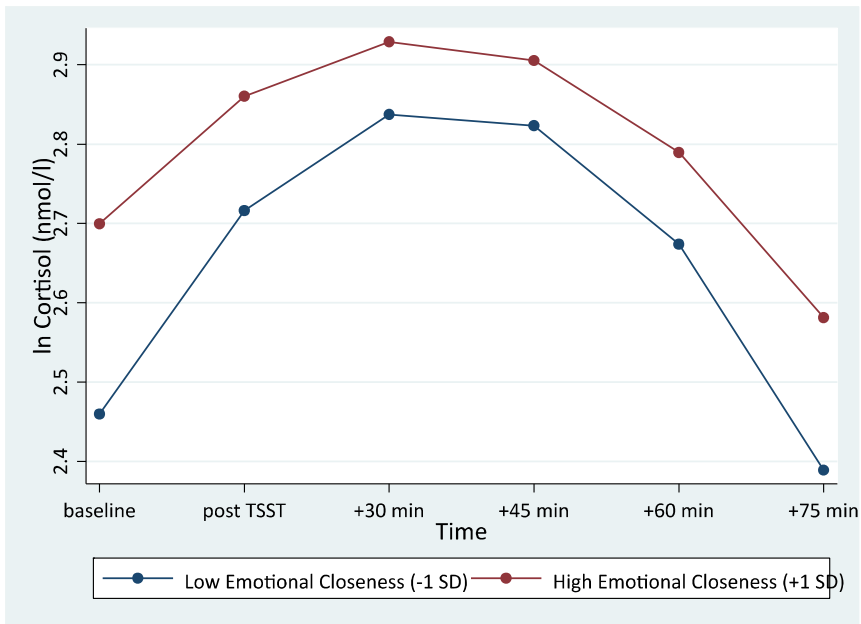
*Figure 9a.* Cortisol responses were heightened for individuals with high NA reactivity compared to individuals with low NA reactivity.



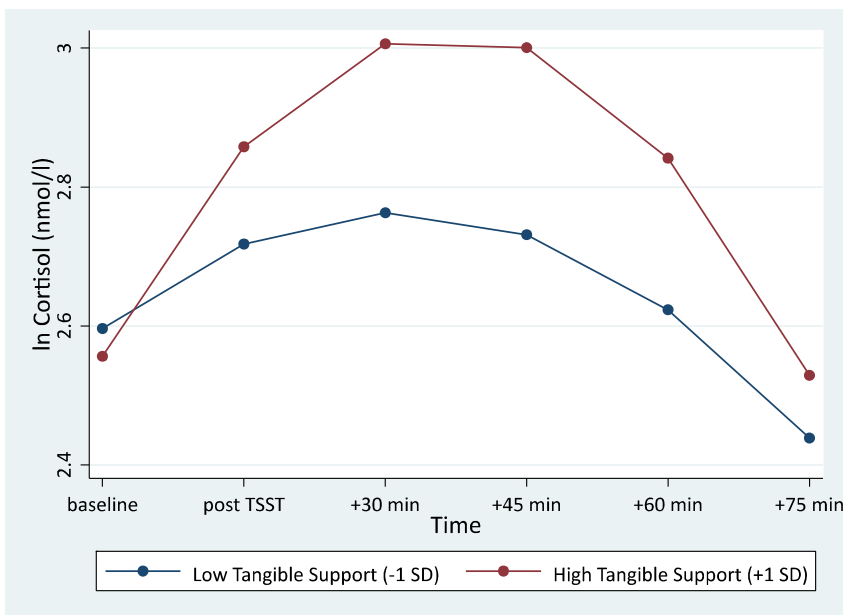
*Figure 9b.* Cortisol responses were heightened for individuals with high fear reactivity compared to individuals with low fear reactivity.



*Figure 9c.* Cortisol responses were heightened for individuals with high guilt reactivity compared to individuals with low guilt reactivity.



*Figure 10a.* Cortisol responses were attenuated for individuals with less emotional closeness compared to individuals with more emotional closeness.



*Figure 10b.* Cortisol responses were attenuated for individuals with less tangible support compared to individuals with more tangible support.

## References

- Aggarwal, B. B. (2010). Targeting inflammation-induced obesity and metabolic diseases by curcumin and other nutraceuticals. *Annual review of nutrition*, 30(1), 173-199.
- Armbruster, D., Mueller, A., Strobel, A., Lesch, K., Brocke, B., & Kirschbaum, C. (2011). Predicting cortisol stress responses in older individuals: Influence of serotonin receptor 1A gene (HTR1A) and stressful life events. *Hormones and Behavior*, 60(1), 105-111.
- Ashman, S. B., Dawson, G., Panagiotides, H., Yamada, E., & Wilkinson, C. W. (2002). Stress hormone levels of children of depressed mothers. *Development and Psychopathology*, 14(2), 333-349.
- Bae, D., Wickrama, K. A. S., & O'Neal, C. W. (2014). Social consequences of early socioeconomic adversity and youth BMI trajectories: gender and race/ethnicity differences. *Journal of Adolescence*, 37(6), 883-892.
- Bajaj, A., John-Henderson, N. A., Cundiff, J. M., Marsland, A. L., Manuck, S. B., & Kamarck, T. W. (in press). Daily social interactions, close relationships, and systemic inflammation in two samples: Healthy middle-aged and older adults. *Brain, Behavior, and Immunity*.
- Baumeister, D., Akhtar, R., Ciufolini, S., Pariante, C. M., & Mondelli, V. (in press). Childhood trauma and adulthood inflammation: a meta-analysis of peripheral C-reactive protein, interleukin-6 and tumour necrosis factor- $\alpha$ . *Molecular psychiatry*.
- Berkman, L. F., & Syme, S. L. (1979). Social networks, host resistance, and mortality: a nine-year follow-up study of Alameda County residents. *American journal of epidemiology*, 109(2), 186-204.

- Bierhaus, A., Wolf, J. , Andrassy, M., Rohleder, N., Humpert, P. M., Petrov, D., . . . Nawroth, P. P. (2003). A mechanism converting psychosocial stress into mononuclear cell activation. *Proceedings of the National Academy of Sciences, 100*(4), 1920-1925.
- Blakemore, S. J., & Mills, K. L. (2014). Is adolescence a sensitive period for sociocultural processing? *Annu Rev Psychol, 65*, 187-207.
- Bogdan, R., Williamson, D. E., & Hariri, A. R. (2012). Mineralocorticoid receptor Iso/Val (rs5522) genotype moderates the association between previous childhood emotional neglect and amygdala reactivity. *American Journal of Psychiatry, 169*(5), 515-522.
- Bosch, J. A., Veerman, E. C., de Geus, E. J., & Proctor, G. B. (2011).  $\alpha$ -Amylase as a reliable and convenient measure of sympathetic activity: don't start salivating just yet! *Psychoneuroendocrinology, 36*(4), 449-453.
- Bosch, N. M., Riese, H., Reijneveld, S. A., Bakker, M. P., Verhulst, F. C., Ormel, J., & Oldehinkel, A. J. (2012). Timing matters: Long term effects of adversities from prenatal period up to adolescence on adolescents' cortisol stress response. The TRAILS study. *Psychoneuroendocrinology, 37*(9), 1439-1447.
- Boyer, B. P., & Nelson, J. A. (2015). Longitudinal associations of childhood parenting and adolescent health: The mediating influence of social competence. *Child Development, 86*(3), 828-843.
- Bruce, J, Fisher, P. A., Pears, K. C., & Levine, S. (2009). Morning cortisol Levels in preschool-aged foster children: Differential effects of maltreatment type. *Developmental Psychobiology, 51*(1), 14-23.

- Brydon, L., & Steptoe, A. (2005). Stress-induced increases in interleukin-6 and fibrinogen predict ambulatory blood pressure at 3-year follow-up. *Journal of hypertension*, 23(5), 1001-1007.
- Bugental, D. B., Martorell, G. A., & Barraza, V. (2003). The hormonal costs of subtle forms of infant maltreatment. *Hormones and Behavior*, 43(1), 237-244.
- Burton, C. L., Bonanno, G. A., & Hatzenbuehler, M. L. (2014). Familial social support predicts a reduced cortisol response to stress in sexual minority young adults. *Psychoneuroendocrinology*, 47, 241-245.
- Buyse, D. J., Reynolds III, C. F., Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Research*, 28(2), 193-213.
- Campos, B., & Shenhav, S. (2014). Relationships in Multicultural Contexts *Perspectives on the Intersection of Multiculturalism and Positive Psychology* (pp. 93-105). Netherlands: Springer.
- Carpenter, L. L., Carvalho, J. P., Tyrka, A. R., Wier, L. M., Mello, A. F., Mello, M. F., . . . Price, L. H. (2007). Decreased adrenocorticotropic hormone and cortisol responses to stress in healthy adults reporting significant childhood maltreatment. *Biological Psychiatry*, 62(10), 1080-1087.
- Carpenter, L. L., Gawuga, C. E., Tyrka, A. R., Lee, J. K., Anderson, G. M., & Price, L. H. (2010). Association between plasma IL-6 response to acute stress and early-life adversity in healthy adults. *Neuropsychopharmacology*, 35(13), 2617-2623.

- Carpenter, L. L., Shattuck, T. T., Tyrka, A. R., Geraciotti, T. D., & Price, L. H. (2011). Effect of childhood physical abuse on cortisol stress response. *Psychopharmacology (Berl)*, 214(1), 367-375.
- Carpenter, L. L., Tyrka, A. R., Ross, N. S., Khoury, L., Anderson, G. M., & Price, L. H. (2009). Effect of childhood emotional abuse and age on cortisol responsivity in adulthood. *Biological Psychiatry*, 66(1), 69-75.
- Carroll, J. E., Gruenewald, T. L., Taylor, S. E., Janicki-Deverts, D., Matthews, K. A., & Seeman, T. E. (2013). Childhood abuse, parental warmth, and adult multisystem biological risk in the Coronary Artery Risk Development in Young Adults study. *Proceedings of the National Academy of Sciences*, 110(42), 17149-17153.
- Carroll, J. E., Low, C. A., Prather, A. A., Cohen, S., Fury, J. M., Ross, D. C., & Marsland, A. L. (2011). Negative affective responses to a speech task predict changes in interleukin (IL)-6. *Brain, Behavior, and Immunity*, 25(2), 232-238.
- Cecil, C. A. M., Viding, E., McCrory, E. J., & Gregory, A. M. (2015). Distinct mechanisms underlie associations between forms of childhood maltreatment and disruptive nocturnal behaviors. *Developmental neuropsychology*, 40(3), 181-199.
- Champaneri, S. , Xu, X., Carnethon, M. R., Bertoni, A. G., Seeman, T., DeSantis, A. S., . . . Golden, S. H. (2013). Dirunal salivary cortisol is associated with body mass index and waist circumference: The multiethnic study of atherosclerosis. *Obesity*, 21(1), E56-E63.
- Chapman, D. P., Liu, Y., Presley-Cantrell, L. R., Edwards, V. J., Wheaton, A. G., Perry, G. S., & Croft, J. B. (2013). Adverse childhood experiences and frequent insufficient sleep in 5 U.S. states, 2009: A retrospective cohort study. *BMC Public Health*, 13(3), 1-9.

- Chapman, D. P., Whaton, A. G. , Anda, R. F., Croft, J. B., Edwards, V. J., Liu, Y., . . . Perry, G. S. (2011). Adverse childhood experiences and sleep disturbances in adults. *Sleep Medicine, 12*(8), 773-779.
- Chapman, D. P., Wheaton, A. G., Anda, R. F., Croft, J. B., Edwards, V. J., Liu, Y., . . . Perry, G. S. (2011). Adverse childhood experiences and sleep disturbances in adults. *Sleep Medicine, 12*(8), 773-779.
- Charbonneau, A. M., Mezulis, A. H., & Hyde, J. S. (2009). Stress and emotional reactivity as explanations for gender differences in adolescents' depressive symptoms. *J Youth Adolesc, 38*(8), 1050-1058.
- Chen, E., Hanson, M. D., Paterson, L. Q., Griffin, M. J., Walker, H. A., & Miller, G. E. (2006). Socioeconomic status and inflammatory processes in childhood asthma: the role of psychological stress. *Journal of Allergy and Clinical Immunology, 117*(5), 1014-1020.
- Chen, E., Langer, D. A., Raphaelson, Y. E., & Matthews, K. A. (2004). Socioeconomic status and health in adolescents: the role of stress interpretations. *Child Development, 75*(4), 1039-1052.
- Chen, E., & Matthews, K. A. (2001). Cognitive appraisal biases: An approach to understanding the relation between socioeconomic status and cardiovascular reactivity in children. *Annals of Behavioral Medicine, 23*(2), 101-111.
- Chiang, J. J., Eisenberger, N. I., Seeman, T. E., & Taylor, S. E. (2012). Negative and competitive social interactions are related to heightened proinflammatory cytokine activity. *Proceedings of the National Academy of Sciences, 109*(6), 1878-1882.
- Cho, H. J., Seeman, T. E., Kiefe, C. I., Lauderdale, D. S., & Irwin, M.R. (2015). Sleep disturbance and longitudinal risk of inflammation: Moderating influences of social

- integration and social isolation in the Coronary Artery Risk Development in Young Adults (CARDIA) study. *Brain, Behavior, and Immunity*, 46, 319-326.
- Cohen, S., Janicki-Deverts, D., Doyle, W. J., Miller, G. E., Frank, E., Rabin, B. S., & Turner, R. B. (2012). Chronic stress, glucocorticoid receptor resistance, inflammation, and disease risk. *Proceedings of the National Academy of Sciences*, 109(16), 5995-5999.
- Cohen, S., Janicki-Deverts, D., Chen, E., & Matthews, K. A. (2010). Childhood socioeconomic status and adult health. *Annals of the New York Academy of Sciences*, 1186(1), 37-55.
- Cole, S. W., Arevalo, J. M. G., Takahashi, R., Sloan, E. K., Lutgendorf, S. K., Sood, A. K., . . . Seeman, T. E. (2010). Computational identification of gene–social environment interaction at the human IL6 locus. *Proceedings of the National Academy of Sciences*, 107(12), 5681-5686.
- Collins, W. A., & Russell, G. (1991). Mother-child and father-child relationships in middle childhood and adolescence: A developmental analysis. *Developmental Review*, 11(2), 99-136.
- Collins, W. A., & Steinberg, L. (2006). Adolescent development in interpersonal context. *Handbook of child psychology*.
- Cook, S., Weitzman, M., Auinger, P., Nguyen, M., & Dietz, W. H. (2003). Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988-1994. *Archives of pediatrics & adolescent medicine*, 157(8), 821-827.
- Cooley-Quille, M., & Lorion, R. (1999). Adolescents' exposure to community violence: Sleep and psychophysiological functioning. *Journal of Community Psychology*, 27(4), 367-375.

- Crosswell, A. D., Bower, J. E., & Ganz, P. A. (2014). Childhood adversity and inflammation in breast cancer survivors. *Psychosomatic Medicine*, 76(3), 208.
- Cui, M., & Fincham, F. D. (2010). The differential effects of parental divorce and marital conflict on young adult romantic relationships. *Personal Relationships*, 17(3), 331-343.
- Cutrona, C. E., & Russell, D. (1987). The provisions of social relationships and adaptation to stress. In W. H. Jones & D. Perlman (Eds.), *Advances in Personal Relationships* (Vol. 1, pp. 37-67). Greenwich, CT: JAI Press.
- Dahl, R. E., & Lewin, D. S. (2002). Pathways to adolescent health sleep regulation and behavior. *Journal of Adolescent Health*, 31(6), 175-184.
- Danese, A., Pariante, C. M., Caspi, A., Taylor, A., & Poulton, R. (2007). Childhood maltreatment predicts adult inflammation in a life-course study. *Proceedings of the National Academy of Sciences*, 104(4), 1319-1324. doi: 10.1073/pnas.0610362104
- Dannlowski, U., Stuhrmann, A., Beutelmann, V., Zwanzger, P., Lenzen, T., Grotegerd, D., . . . Kugel, H. . (2012). Limbic scars: long-term consequences of childhood maltreatment revealed by functional and structural magnetic resonance imaging. *Biological Psychiatry*, 71(4), 286-293.
- Davies, P. T., & Cicchetti, D. (2004). Toward an integration of family systems and developmental psychopathology approaches. *Development and Psychopathology*, 16, 477-481.
- Davies, P. T., Sturge-Apple, M. L., Cicchetti, D., Manning, L. G., & Zale, E. (2009). Children's patterns of emotional reactivity to conflict as explanatory mechanisms in links between interpartner aggression and child physiological functioning. *Journal of Child Psychology and Psychiatry*, 50(11), 1384-1391.

- De Bellis, M. D. (2001). Developmental traumatology: The psychobiological development of maltreated children and its implications for research, treatment, and policy. *Development and Psychopathology*, 13(03), 539-564.
- Del Giudice, M., Ellis, B. J., & Shirtcliff, E. A. (2011). The adaptive calibration model of stress responsivity. *Neuroscience & Biobehavioral Reviews*, 35(7), 1562-1592.
- Denson, T. F., Spanovic, M., & Miller, N. (2009). Cognitive appraisals and emotions predict cortisol and immune responses: a meta-analysis of acute laboratory social stressors and emotion inductions. *Psychological Bulletin*, 135(6), 823-853. doi: 10.1037/a0016909
- Dickerson, S. S., & Kemeny, M. E. (2004). Acute stressors and cortisol responses: a theoretical integration and synthesis of laboratory research. *Psychological Bulletin*, 130(3), 355.
- Dickerson, S. S., Kemeny, M. E., Aziz, N., Kim, K. H., & Fahey, J. L. (2004). Immunological effects of induced shame and guilt. *Psychosomatic Medicine*, 66(1), 124-131.
- Dietz, L. J., Stoyak, S., Melhem, N., Porta, G., Matthews, K. A., Payne, M. Walker., & Brent, D. A. (2013). Cortisol response to social stress in parentally bereaved youth. *Biological Psychiatry*, 73(4), 379-387.
- Doane, L. D., & Zeiders, K. H. (2014). Contextual moderators of momentary cortisol and negative affect in adolescents' daily lives. *Journal of Adolescent Health*, 54(5), 536-542.
- Dowd, J. B., Simanek, A. M., & Aiello, A. E. (2009). Socio-economic status, cortisol and allostatic load: a review of the literature. *International Journal of Epidemiology*, 38(5), 1297-1309.
- Drake, E. C., Sladek, M. R., & Doane, L. D. (2016). Daily cortisol activity, loneliness, and coping efficacy in late adolescence A longitudinal study of the transition to college. *International Journal of Behavioral Development*, 40(4), 334-345.

- Eisenberger, N. I., Taylor, S. E., Gable, S. L., Hilmert, C. J., & Lieberman, M. D. (2007). Neural pathways link social support to attenuated neuroendocrine stress responses. *Neuroimage*, 35(4), 1601-1612.
- El-Sheikh, M., Buckhalt, J. A., Mize, J., & Acebo, B. (2006). Marital conflict and disruption of children's sleep. *Child Development*, 77(1), 31-43.
- El-Sheikh, M., Erath, S. A., Buckhalt, J. A., Granger, D. A., & Mize, J. (2008). Cortisol and children's adjustment: The moderating role of sympathetic nervous system activity. *Journal of Abnormal Child Psychology*, 36(4), 601-611.
- El-Sheikh, M. (2005). The role of emotional responses and physiological reactivity in the marital conflict-child functioning link. *Journal of Child Psychology and Psychiatry*, 46(11), 1191-1199.
- Ellis, B. J., Essex, M. J., & Boyce, W. T. (2005). Biological sensitivity to context: II. Empirical explorations of an evolutionary-developmental theory. *Development and Psychopathology*, 17(02), 303-328.
- Engert, V., Buss, C., Khalili-Mahani, N., Wadiwalla, M., Dedovic, K., & Pruessner, J. C. (2010). Investigating the association between early life parental care and stress responsivity in adulthood. *Developmental neuropsychology*, 35(5), 570-581.
- Engert, V., Efanov, S. I., Dedovic, K., Duchesne, A., Dagher, A., & Pruessner, J. C. (2010). Perceived early-life maternal care and the cortisol response to repeated psychosocial stress. *Journal of Psychiatry & Neuroscience*, 35(6), 370.
- Essex, M. J., Klein, M. H., Cho, E., & Kalin, N. H. (2002). Maternal stress beginning in infancy may sensitize children to later stress exposure: effects on cortisol and behavior. *Biological Psychiatry*, 52(8), 776-784.

- Fagundes, C. P., Glaser, R., & Kiecolt-Glaser, J. K. (2013). Stressful early life experiences and immune dysregulation across the lifespan. *Brain, Behavior, and Immunity*, 27(1), 8-12.  
doi: 10.1016/j.bbi.2012.06.014
- Felitti, V. J., Anda, R. F., Nordenberg, D., Williamson, D. F., Spitz, A. M., Edwards, V., . . . Marks, J. S. (1998). Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: The Adverse Childhood Experiences (ACE) Study. *American Journal of Preventive Medicine*, 14(4), 245-258.
- Fernald, L. C. H., Burke, H. M., & Gunnar, M. R. (2008). Salivary cortisol levels in children of low-income women with high depressive symptomatology. *Development and Psychopathology*, 20(2), 423.
- Ferrie, J. E., Kivimäki, M., Akbaraly, T. N., Singh-Manoux, A., Miller, M. A., Gimeno, D., . . . Shipley, M. J. (2013). Associations between change in sleep duration and inflammation: findings on C-reactive protein and interleukin 6 in the Whitehall II Study. *American journal of epidemiology*, 178(6), 956-961.
- Fonzo, G. A., Ramsawh, H. J., Flagan, T. M., Simmons, A. N., Sullivan, S. G., Allard, C. B., . . . Stein, M. B. (2016). Early life stress and the anxious brain: evidence for a neural mechanism linking childhood emotional maltreatment to anxiety in adulthood. *Psychological Medicine*, 46(05), 1037-1054.
- Fosco, G. M., Caruthers, A. S., & Dishion, T. J. (2012). A six-year predictive test of adolescent family relationship quality and effortful control pathways to emerging adult social and emotional health. *Journal of Family Psychology*, 26(4), 565-575.

- Freeberg, A. L., & Stein, C. H. (1996). Felt obligation towards parents in Mexican-American and Anglo-American young adults. *Journal of Social and Personal Relationships*, 13(3), 457-471.
- Frey, D. J., Fleshner, M., & Wright Jr., K. P. (2007). The effects of 40 hours of total sleep deprivation on inflammatory markers in healthy young adults. *Brain, Behavior, & Immunity*, 21(8), 1050-1057.
- Friedman, E. M., Hayne, M. S. , Love, G. D. , Urry, H. L., Rosenkranz, M. A. , Davidson, R. J. , . . . Ryff, C. D. . (2005). Social relationships, sleep quality, and interleukin-6 in aging women. *Proceedings of the National Academy of Sciences*, 102(51), 18757-18762.
- Fries, A. B. W., Shirtcliff, E. A., & Pollak, S. D. (2008). Neuroendocrine dysregulation following early social deprivation in children. *Developmental Psychobiology*, 50(6), 588-599.
- Fuligni, A. J., Telzer, E. H., Bower, J., Cole, S. W., Kiang, L., & Irwin, M. R. (2009). A preliminary study of daily interpersonal stress and C-reactive protein levels among adolescents from Latin American and European backgrounds. *Psychosomatic Medicine*, 71(3), 329-333.
- Gaab, J., Rohleder, N., Nater, U. M., & Ehlert, U. (2005). Psychological determinants of the cortisol stress response: the role of anticipatory cognitive appraisal. *Psychoneuroendocrinology*, 30(6), 599-610.
- Galambos, N. L., Barker, E. T., & Almeida, D. M. (2003). Parents do matter: Trajectories of change in externalizing and internalizing problems in early adolescence. *Child Development*, 74(2), 578-594.

- Gallicchio, L., & Kalesan, B. (2009). Sleep duration and mortality: a systematic review and meta-analysis. *Journal of Sleep Research*, 18(2), 148-158.
- Gatt, J. M., Nemeroff, C. B., Dobson-Stone, C., Paul, R. H. , Bryant, R. A., Schofield, P. R., . . . Williams, L. M. (2009). Interactions between BDNF Val66Met polymorphism and early life stress predict brain and arousal pathways to syndromal depression and anxiety. *Molecular psychiatry*, 14(7), 681-695.
- Gelaye, B., Kajeepeta, S., Zhong, Q. Y., Borba, C. P. C., Rondon, M. B., Sánchez, S. E., . . . Williams, M. A. (2015). Childhood abuse is associated with stress-related sleep disturbance and poor sleep quality in pregnancy. *Sleep Medicine*, 16(10), 1274-1280.
- Glaser, J. P., van Os, J., Portegijs, P. J. M., & Myin-Germeys, I. (2006). Childhood trauma and emotional reactivity to daily life stress in adult frequent attenders of general practitioners. *Journal of Psychosomatic Research*, 61(2), 229-236.
- Glei, D. A., Goldman, N., Ryff, C. D., Lin, Y. H., & Weinstein, M. (2012). Social relationships and inflammatory markers: An analysis of Taiwan and the US. *Social Science & Medicine*, 74(12), 1891-1899.
- Glezer, I., & Rivest, S. (2004). Glucocorticoids: protectors of the brain during innate immune responses. *The Neuroscientist*, 10(6), 538-552.
- Glod, C. A., Teicher, M. H., Hartman, C. R., & Harakal, T. (1997). increased nocturnal activity and impaired sleep maintenance in abused children. *Journal of the American Academy of Child & Adolescent Psychiatry*, 36(9), 1236-1243.
- Godinet, M. T., Li, F., & Berg, T. (2014). Early childhood maltreatment and trajectories of behavioral problems: Exploring gender and racial differences. *Child Abuse & Neglect*, 38(3), 544-556.

- Goel, N., Kim, H., & Lao, R. P. (2005). Gender differences in polysomnographic sleep in young healthy sleepers. *Chronobiology International*, 22(5), 905-915.
- Gouin, J. , Glaser, R., Malarkey, W. B., Beversdorf, D., & Kiecolt-Glaser, J. K. (2012). Childhood abuse and inflammatory responses to daily stressors. *Annals of Behavioral Medicine*, 44(2), 287-292.
- Gouin, J. P., Glaser, R., Loving, T. J., Malarkey, W. B., Stowell, J., Houts, C., & Kiecolt-Glaser, J. K. (2009). Attachment avoidance predicts inflammatory responses to marital conflict. *Brain, Behavior, and Immunity*, 23(7), 898-904.
- Gramer, M., & Supp, N. (2014). Social support and prolonged cardiovascular reactivity: the moderating influence of relationship quality and type of support. *Biological Psychology*, 101, 1-8.
- Granger, D. A., Blair, C., Willoughby, M. T., Kivlighan, K. T., Hibel, L. C., Fortunato, C. K., & Wiegand, L. E. (2007). Individual differences in salivary cortisol and alpha-amylase in mothers and their infants: Relation to tobacco smoke exposure. *Developmental Psychobiology*, 49(7), 692-701.
- Greenfield, E. A., Lee, C., Friedman, E. L., & Springer, K. W. (2011). Childhood abuse as a risk factor for sleep problems in adulthood: Evidence from a U.S. national study. *Annals of Behavioral Medicine*, 42(2), 245-256.
- Grisanti, L. A., Woster, A. P., Dahlman, J., Sauter, E. R., Combs, C. K., & Porter, J. E. (2011).  $\alpha$ 1-adrenergic receptors positively regulate Toll-like receptor cytokine production from human monocytes and macrophages. *Journal of Pharmacology and Experimental Therapeutics*, 338(2), 648-657.

- Grusec, J. E. (2011). Socialization processes in the family: Social and emotional development. *Annu Rev Psychol*, 62, 243-269.
- Gunnar, M. R., & Donzella, B. (2002). Social regulation of the cortisol levels in early human development. *Psychoneuroendocrinology*, 27(1), 199-220.
- Haack, M., Sanchez, E., & Mullington, J. M. (2007). Elevated inflammatory markers in response to prolonged sleep restriction are associated with increased pain experience in healthy volunteers. *Sleep*, 2007(30), 9.
- Hall, M. H., Lee, L., & Matthews, K. A. (2015). Sleep duration during the school week is associated with C-reactive protein risk groups in healthy adolescents. *Sleep Medicine*, 16(1), 73-78.
- Hammen, C. (1991). Generation of stress in the course of unipolar depression. *Journal of Abnormal Psychology*, 100(4), 555-561.
- Hammen, C. (2005). Stress and depression. *Annual review of clinical psychology*, 1, 293-319.
- Hawkey, L. C., & Cacioppo, J. T. (2010). Loneliness matters: a theoretical and empirical review of consequences and mechanisms. *Annals of Behavioral Medicine*, 40(2), 218-227.
- Hazel, N. A., Hammen, C., Brennan, P. A., & Najman, J. (2008). Early childhood adversity and adolescent depression: the mediating role of continued stress. *Psychological Medicine*, 38(04), 581-589.
- Heider, D., Matschinger, H., Bernert, S., Alonso, J., & Angermeyer, M. C. (2006). Relationship between parental bonding and mood disorder in six European countries. *Psychiatry Research*, 143(1), 89-98.

- Heim, C., & Binder, E. B. (2012). Current research trends in early life stress and depression: Review of human studies on sensitive periods, gene–environment interactions, and epigenetics. *Experimental Neurology*, 233(1), 102-111.
- Heim, C., Newport, D. J., Heit, S., Graham, Y. P., Wilcox, M., Bonsall, R., . . . Nemeroff, C. B. (2000). Pituitary-adrenal and autonomic responses to stress in women after sexual and physical abuse in childhood. *Journal of the American Medical Association*, 284(5), 592-597.
- Heim, C., Newport, D. J., Wagner, D., Wilcox, M. M., Miller, A. H., & Nemeroff, C. B. (2002). The role of early adverse experience and adulthood stress in the prediction of neuroendocrine stress reactivity in women: a multiple regression analysis. *Depression and Anxiety*, 15(3), 117-125.
- Helsen, M., Vollebergh, W., & Meeus, W. (2000). Social support from parents and friends and emotional problems in adolescence. *J Youth Adolesc*, 29(3), 319-335.
- Herrera, C., & Dunn, J. (1997). Early experiences with family conflict: Implications for arguments with a close friend. *Developmental Psychology*, 33(5), 869-881.
- Hill-Soderlund, A. L., Holochwost, S. J., Willoughby, M. T., Granger, D. A., Gariépy, J. L., Mills-Koonce, W. R., & Cox, M. J. (2015). The developmental course of salivary alpha-amylase and cortisol from 12 to 36 months: Relations with early poverty and later behavior problems. *Psychoneuroendocrinology*, 52, 311-323.
- Hinojosa-Laborde, C., Chapa, I., Lange, D., & Haywood, J. R. (1999). Gender differences in sympathetic nervous system regulation. *Clinical and Experimental Pharmacology and Physiology*, 26(2), 122-126.

- Ho, R. T. H., Fong, T. C. T., Chan, C. K. P., & Chan, C. L. W. (2013). The associations between diurnal cortisol patterns, self-perceived social support, and sleep behavior in Chinese breast cancer patients. *Psychoneuroendocrinology*, 38(10), 2337-2342.
- Hong, S., Mills, P. J., Lored, J. S., Adler, K. A., & Dimsdale, J. E. (2005). The association between interleukin-6, sleep, and demographic characteristics. *Brain, Behavior, & Immunity*, 19(2), 165-172.
- Hosang, G. M., Johnson, S. L., Kiecolt-Glaser, J. K., Di Gregorio, M. P., Lambert, D. R., Bechtel, M. A., . . . Glaser, R. (2013). Gender specific association of child abuse and adult cardiovascular disease in a sample of patients with Basal Cell Carcinoma. *Child Abuse & Neglect*, 37(6), 374-379.
- Hostinar, C. E., & Gunnar, M. R. (2013). The developmental psychobiology of stress and emotion in childhood. In I. B. Weiner, D. K. Freedheim & M. Lerner (Eds.), *Handbook of Psychology*. Hoboken, NJ: Wiley.
- Hostinar, C. E., Sullivan, R. M., & Gunnar, M. R. (2014). Psychobiological mechanisms underlying the social buffering of the hypothalamic–pituitary–adrenocortical axis: A review of animal models and human studies across development. *Psychological Bulletin*, 140(1), 256-582.
- Howren, M. B., Lamkin, D. M., & Suls, J. (2009). Associations of depression with C-reactive protein, IL-1, and IL-6: A meta-analysis. *Psychosomatic Medicine*, 71(2), 171-186.
- Hughes, B., & Curtis, R. (2000). Quality and quantity of social support as differential predictors of cardiovascular reactivity. *The Irish Journal of Psychology*, 21(1-2), 16-31.
- Hughes, B. M. (2005). Support as intimidation: When social interaction elevates stress-related blood pressure. *The Irish Journal of Psychology*, 26(1-2), 75-86.

- Hughes, B. M. (2007). Social support in ordinary life and laboratory measures of cardiovascular reactivity: Gender differences in habituation-sensitization. *Annals of Behavioral Medicine*, 34(2), 166-176.
- Infurna, F. J., Rivers, C. T., Reich, J., & Zautra, A. J. (2015). Childhood trauma and personal mastery: Their influence on emotional reactivity to everyday events in a community sample of middle-aged adults. *PLoS One*, 10(4), e0121840.
- Irwin, M. R., & Cole, S. W. (2011). Reciprocal regulation of the neural and innate immune systems. *Nature Reviews Immunology*, 11(9), 625-632. doi: 10.1038/nri3042
- Irwin, M. R., Wang, M., Ribeiro, D., Cho, H.J., Olmstead, R. , Breen, E. C., . . . Cole, S. W. (2008). Sleep loss activates cellular inflammatory signaling. *Biological Psychiatry*, 64(6), 538-540.
- Jaremka, L. M., Fagundes, C. P., Peng, J., Bennett, J. M., Glaser, R., Malarkey, W. B., & Kiecolt-Glaser, J. K. (2013). Loneliness promotes inflammation during acute stress. *Psychological Science*, 24(7), 1089-1097.
- John-Henderson, N. A., Stellar, J.E., Mendoza-Denton, R., & Francis, D. D. (2015). Socioeconomic status and social support: Social support Reduces inflammatory reactivity for individuals whose early-life socioeconomic status was low. *Psychological Science*, 26(10), 1620-1629.
- Johnson, J. G., Cohen, P., Gould, M. S., Kasen, S., Brown, J. S., & Brook, J. S. (2002). Childhood adversities, interpersonal difficulties, and risk for suicide attempts during late adolescence and early adulthood. *Archives of General Psychiatry*, 59(8), 741-749.
- Joormann, J., & Vanderlind, W. M. (2014). Emotion regulation in depression the role of biased cognition and reduced cognitive control. *Clinical Psychological Science*, 2(4), 402-421.

- Kajeepeta, S., Gelaye, B., Jackson, C. L., & Williams, M. A. (2015). Adverse childhood experiences are associated with adult sleep disorders: a systematic review. *Sleep Medicine, 16*(3), 320-330.
- Kamiya, Y., Doyle, M., Henretta, J. C., & Timonen, V. (2014). Early-life circumstances and later-life loneliness in Ireland. *The Gerontologist, 54*(5), 773-783.
- Kapoor, A., Petropoulos, S., & Matthews, S. G. (2008). Fetal programming of hypothalamic–pituitary–adrenal (HPA) axis function and behavior by synthetic glucocorticoids. *Brain Research Reviews, 57*(2), 586-595.
- Keeshin, B. R., Strawn, J. R., Out, D., Granger, D. A., & Putnam, F. W. (2015). Elevated salivary alpha amylase in adolescent sexual abuse survivors with posttraumatic stress disorder symptoms. *Journal of child and adolescent psychopharmacology, 25*(4), 344-350.
- Khera, A., McGuire, D. K., Murphy, S. A., Stanek, H. G., Das, S. R., Vongpatanasin, W., . . . de Lemos, J. A. (2005). Race and gender differences in C-reactive protein levels. *Journal of the American College of Cardiology, 46*(3), 464-469.
- Kiecolt-Glaser, J. K., Gouin, J. P., Weng, N., Malarkey, W. B., Beversdorf, D. Q., & Glaser, R. (2011). Childhood adversity heightens the impact of later-life caregiving stress on telomere length and inflammation. *Psychosomatic Medicine, 73*(1), 16-22.
- Kiecolt-Glaser, J. K., Loving, T. J., Stowell, J. R., Malarkey, W. B., Lemeshow, S., Dickinson, S. L., & Glaser, R. (2005). Hostile marital interactions, proinflammatory cytokine production, and wound healing. *Archives of General Psychiatry, 62*(12), 1377-1384.

- Kirschbaum, C., Klauer, T., Filipp, S. H., & Hellhammer, D. H. (1995). Sex-specific effects of social support on cortisol and subjective responses to acute psychological stress. *Psychosomatic Medicine*, 57(1), 23-31.
- Kirschbaum, C., Pirke, K. M., & Hellhammer, D. H. (1993). The 'Trier Social Stress Test'—a tool for investigating psychobiological stress responses in a laboratory setting. *Neuropsychobiology*, 28(1-2), 76-81.
- Klahr, A. M., Rueter, M. A., McGue, M., Iacono, W. G., & Burt, S. A. (2011). The relationship between parent-child conflict and adolescent antisocial behavior: Confirming shared environmental mediation. *Journal of Abnormal Child Psychology*, 39(5), 683-694.
- Koskenvuo, K., Hublin, C., Partinen, M., Paunio, T., & Koskenvuo, M. (2010). Childhood adversities and quality of sleep in adulthood: A population based study of 26,000 Finns. *Sleep Medicine*, 11(1), 17-22.
- Krackow, E., & Rudolph, K. D. (2008). Life stress and the accuracy of cognitive appraisals in depressed youth. *Journal of Clinical Child & Adolescent Psychology*, 37(2), 376-385.
- Kuebler, U., Wirtz, P. H., Sakai, M., Stemmer, A., Meister, R. E., & Ehlert, U. (2015). Anticipatory cognitive stress appraisal modulates suppression of wound-induced macrophage activation by acute psychosocial stress. *Psychophysiology*, 52(4), 499-508.
- Kuhlman, K. R., Geiss, E. G., Vargas, I., & Lopez-Duran, N. L. (2015). Differential associations between childhood trauma subtypes and adolescent HPA-axis functioning. *Psychoneuroendocrinology*, 54, 103-114.
- Kumari, M., Head, J., Bartley, M., Stansfeld, S., & Kivimaki, M. (2012). Maternal separation in childhood and diurnal cortisol patterns in mid-life: findings from the Whitehall II study. *Psychological Medicine*, 1(1), 1-11.

- Kunz-Ebrecht, S. R., Mohamed-Ali, V., Feldman, P. J., Kirschbaum, C., & Steptoe, A. (2003). Cortisol responses to mild psychological stress are inversely associated with proinflammatory cytokines. *Brain, Behavior, and Immunity*, 17(5), 373-383.
- Lakoski, S. G., Cushman, M., Criqui, M., Rundek, T., Blumenthal, R. S., D'Agostino Jr, R. B., & Herrington, D. M. (2006). Gender and C-reactive protein: data from the Multiethnic Study of Atherosclerosis (MESA) cohort. *American heart journal*, 152(3), 593-598.
- Lansford, J. E., Dodge, K. A., Pettit, G. S., Bates, J. E., Crozier, J., & Kaplow, J. (2002). A 12-year prospective study of the long-term effects of early child physical maltreatment on psychological, behavioral, and academic problems in adolescence. *Archives of pediatrics & adolescent medicine*, 156(8), 824-230.
- Larkin, E. K., Rosen, C. L., Kirchner, H. L., Storfer-Isser, A., Emancipator, J. L., Johnson, N. L., . . . Redline, S. (2005). Variation of C-reactive protein levels in adolescents association with sleep-disordered breathing and sleep duration. *Circulation*, 111(15), 1978-1984.
- Larkin, K. T., Frazer, N. L., & Semenchuk, E. M. (1996). Physiological, affective, and behavioral responses to interpersonal conflict among males from families with different levels of cohesion and adaptability. *Journal of Psychopathology and Behavioral Assessment*, 18(3), 239-254.
- Larkin, K. T., Frazer, N. L., & Wheat, A. L. (2011). Responses to interpersonal conflict among young adults: Influence of family of origin. *Personal Relationships*, 18(4), 657-667.
- Lazarus, R. S. (1966). *Psychological stress and the coping process*. New York: McGraw-Hill.
- Lazarus, R. S., & Folkman, S. (1984). *Stress, appraisal, and coping*. New York: Springer.

- Leitzke, B. T., Hilt, L. M., & Pollak, S. D. (2015). Maltreated youth display a blunted blood pressure response to an acute interpersonal stressor. *Journal of Clinical Child & Adolescent Psychology*, 44(2), 305-313.
- Lerner, J. S., Dahl, R. E., Hariri, A. R., & Taylor, S. E. (2007). Facial expressions of emotion reveal neuroendocrine and cardiovascular stress responses. *Biological Psychiatry*, 61(2), 253-260.
- Libby, P. (2006). Inflammation and cardiovascular disease mechanisms. *The American Journal of Clinical Nutrition*, 83(2), 456S-460S.
- Liu, R. T., & Alloy, L. B. (2010). Stress generation in depression: A systematic review of the empirical literature and recommendations for future study. *Clinical Psychology Review*, 30(5), 582-593.
- Lockley, S. W., Skene, D. J., & Arendt, J. (1999). Comparison between subjective and actigraphic measurement of sleep and sleep rhythms. *Journal of Sleep Research*, 8(3), 175-183.
- Lovallo, W. R. (2013). Early life adversity reduces stress reactivity and enhances impulsive behavior: Implications for health behaviors. *International Journal of Psychophysiology*, 90(1), 8-16.
- .
- Lovejoy, M. C., Graczyk, P. A., O'Hare, E., & Neuman, G. (2000). Maternal depression and parenting behavior: A meta-analytic review. *Clinical Psychology Review*, 20(5), 561-592.
- Luecken, L. J. (1998). Childhood attachment and loss experiences affect adult cardiovascular and cortisol function. *Psychosomatic Medicine*, 60(6), 765-772.

- Luecken, L. J., & Appelhans, B. M. (2006). Early parental loss and salivary cortisol in young adulthood: the moderating role of family environment. *Development and Psychopathology*, 18(01), 295-308.
- Luecken, L. J., Appelhans, B. M., Kraft, A., & Brown, A. (2006). Never far from home: A cognitive-affective model of the impact of early-life family relationships on physiological stress responses in adulthood. *Journal of Social and Personal Relationships*, 23, 189-203.
- Luecken, L. J., Kraft, A., & Hagan, M. J. (2009). Negative relationships in the family-of-origin predict attenuated cortisol in emerging adults. *Hormones and Behavior*, 55(3), 412-417.
- Luecken, L. J., & Roubinov, D. S. (2012). Hostile behavior links negative childhood family relationships to heart rate reactivity and recovery in young adulthood. *International Journal of Psychophysiology*, 84(2), 172-179.
- Luecken, L. J., Roubinov, D. S., & Tanaka, R. (2013). Childhood family environment, social competence, and health across the lifespan. *Journal of Social and Personal Relationships*, 30(2), 171-178.
- Lupien, S. J., McEwen, B. S., Gunnar, M. R., & Heim, C. (2009). Effects of stress throughout the lifespan on the brain, behaviour and cognition. *Nature Reviews Neuroscience*, 10(6), 434-445. doi: 10.1038/nrn2639
- Lupis, S. B., Lerman, M., & Wolf, J. M. (2014). Anger responses to psychosocial stress predict heart rate and cortisol stress responses in men but not women. *Psychoneuroendocrinology*, 49, 84-95.
- MacMillan, H. L., Georgiades, K., Duku, E. K., Shea, A., Steiner, M., Niec, A., . . . Schmidt, L. A. (2009). Cortisol response to stress in female youths exposed to childhood maltreatment: results of the youth mood project. *Biological Psychiatry*, 66(1), 62-68.

- Maier, K. J., Waldstein, S. R., & Synowski, S. J. (2003). Relation of cognitive appraisal to cardiovascular reactivity, affect, and task engagement. *Annals of Behavioral Medicine*, 26(1), 32-41.
- Mallers, M. H., Charles, S. T., Neupert, S. D., & Almeida, D. M. (2010). Perceptions of childhood relationships with mother and father: Daily emotional and stressor experiences in adulthood. *Developmental Psychology*, 46(6), 1651-1661.
- Marsland, A. L., Prather, A. A., Petersen, K. L., Cohen, S., & Manuck, S. B. (2008). Antagonistic characteristics are positively associated with inflammatory markers independently of trait negative emotionality. *Brain, Behavior, and Immunity*, 22(5), 753-761.
- Maruyama, Y., Kawano, A., Okamoto, S., Ando, T., Ishitobi, Y., Tanaka, Y., . . . Higuma, H. (2012). Differences in salivary alpha-amylase and cortisol responsiveness following exposure to electrical stimulation versus the Trier Social Stress Tests. *PLoS One*, 7(7), e39375.
- McCrory, E. J., De Brito, S. A., Kelly, P. A., Bird, G., Sebastian, C. L., Mechelli, A., . . . Viding, E. (2013). Amygdala activation in maltreated children during pre-attentive emotional processing. *The British Journal of Psychiatry*, 202(4), 269-276.
- McDade, T. W., Hawkey, L. C., & Cacioppo, J. T. (2006). Psychosocial and behavioral predictors of inflammation in middle-aged and older adults: the Chicago health, aging, and social relations study. *Psychosomatic Medicine*, 68(3), 376-381.
- McEwen, B. S. (1998). Stress, adaptation, and disease: Allostasis and allostatic load. *Annals of the New York Academy of Sciences*, 840(1), 33-44.

- McLaughlin, K. A., Kubzansky, L. D., Dunn, E. C., Waldinger, R., Vaillant, G., & Koenen, K. C. (2010). Childhood social environment, emotional reactivity to stress, and mood and anxiety disorders across the life course. *Depression and Anxiety*, 27(12), 1087-1094.
- 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 & Biobehavioral Reviews*, 47, 578-591.
- McNamee, E. N. , Griffin, E. W., Ryan, K. M., Ryan, K. J., Heffernan, S., Harkin, A., & Connor, T. J. (2010). Noradrenaline acting at  $\beta$ -adrenoceptors induces expression of IL-1 $\beta$  and its negative regulators IL-1ra and IL-1RII, and drives an overall anti-inflammatory phenotype in rat cortex. *Neuropharmacology*, 59(1-2), 37-48.
- Medina, A. B., Lechuga, D. Y. A., Escandon, O. S., & Moctezuma, J. V. (2014). Update of sleep alterations in depression. *Sleep science*, 7(3), 165-169.
- Medzhitov, R. (2010). Inflammation 2010: new adventures of an old flame. *Cell*, 140(6), 771-776. doi: 10.1016/j.cell.2010.03.006
- Meier-Ewert, H. K. , Ridker, P. M., Rifai, N. , Regan, M. M., Price, N. J. , Dinges, D. F., & Mullington, J. M. (2004). Effect of slepe loss on C-reactive protein, an inflammatory marker of cardiovascular risk. *Journal of the American College of Cardiology*, 43(4), 678-683.
- Mendes, W. B., Blascovich, J., Major, B., & Seery, M. (2001). Challenge and threat responses during downward and upward social comaprison. *European Journal of Social Psychology*, 31, 477-497.

- Mezick, E. J., Matthews, K. A., Hall, M. , Strollo, P. J. Jr., Buysse, D. J., Kamarck, T. W., . . . Reis, S. E. (2008). Influence of race and socioeconomic status on sleep: Pittsburgh SleepSCORE project. *Psychosomatic Medicine*, 70(4), 410-416.
- Midei, A. J., & Matthews, K. A. (2011). Interpersonal violence in childhood as a risk factor for obesity: a systematic review of the literature and proposed pathways. *Obesity Reviews*, 12(5), e159-e172.
- Miller, G. E., & Chen, E. (2010). Harsh family climate in early life presages the emergence of a proinflammatory phenotype in adolescence. *Psychological Science*, 21(6), 848-856.
- Miller, G. E., Chen, E., & Parker, K. J. (2011). Psychological stress in childhood and susceptibility to the chronic diseases of aging: moving toward a model of behavioral and biological mechanisms. *Psychological Bulletin*, 137(6), 959-997. doi: 10.1037/a0024768
- Miller, G. E., Chen, E., & Zhou, E. S. (2007). If it goes up, must it come down? Chronic stress and the hypothalamic-pituitary-adrenocortical axis in humans. *Psychological Bulletin*, 133(1), 25-45.
- Miller, G. E., Cohen, S., & Ritchey, A. K. (2002). Chronic psychological stress and the regulation of pro-inflammatory cytokines: a glucocorticoid-resistance model. *Health Psychology*, 21(6), 531-541.
- Miller, G. E., Rohleder, N., & Cole, S. W. (2009). Chronic interpersonal stress predicts activation of pro-and anti-inflammatory signaling pathways 6 months later. *Psychosomatic Medicine*, 71(1), 57-62.
- Mills, P. J. , von Känel, R., Norman, D. , Natarajan, L., Ziegler, M. G., & Dimsdale, J. E. (2007). Inflammation and sleep in healthy individuals. *Sleep*, 30(6), 729-735.

- Miranda, A. O., Bilot, J. M., Peluso, P. R., Berman, K., & Van Meek, L. G. (2006). Latino families: The relevance of the connection among acculturation, family dynamics, and health for family counseling research and practice. *The Family Journal*, 14(3), 268-273.
- Miyamoto, Y., Boylan, J. M., Coe, C. L., Curhan, K. B., Levine, C. S., Markus, H. R., . . . Ryff, C. D. (in press). Negative emotions predict elevated interleukin-6 in the United States but not in Japan. *Brain, Behavior, and Immunity*.
- Moons, W. G., Eisenberger, N. I., & Taylor, S. E. (2010). Anger and fear responses to stress have different biological profiles. *Brain, Behavior, and Immunity*, 24(2), 215-219.
- Moons, W. G., & Shields, G. S. (2015). Anxiety, not anger, induces inflammatory activity: An avoidance/approach model of immune system activation. *Emotion*, 15(4), 463-476.
- Nater, U. M., La Marca, R., Florin, L., Moses, A., Langhans, W., Koller, M. M., & Ehlert, U. (2006). Stress-induced changes in human salivary alpha-amylase activity—associations with adrenergic activity. *Psychoneuroendocrinology*, 31(1), 49-58.
- Nater, U. M., & Rohleder, N. (2009). Salivary alpha-amylase as a non-invasive biomarker for the sympathetic nervous system: Current state of research. *Psychoneuroendocrinology*, 34(4), 486-496.
- Nater, U. M., Rohleder, N., Gaab, J., Berger, S., Jud, A., Kirschbaum, C., & Ehlert, U. (2005). Human salivary alpha-amylase reactivity in a psychosocial stress paradigm. *International Journal of Psychophysiology*, 55(3), 333-342.
- Nausheen, B., Gidron, Y., Gregg, A., Tissarchondou, H. S., & Peveler, R. (2007). Loneliness, social support and cardiovascular reactivity to laboratory stress. *Stress*, 10(1), 37-44.

- Niskanen, L., Laaksonen, D. E., Nyyssönen, K., Punnonen, K., Valkonen, V. P., Fuentes, R., . . . Salonen, J. T. (2004). Inflammation, abdominal obesity, and smoking as predictors of hypertension. *Hypertension*, 44(6), 859-865.
- Norman, R. E., Byambaa, M., De, R., Butchart, A., Scott, J., & Vos, T. (2012). The long-term health consequences of child physical abuse, emotional abuse, and neglect: A systematic review and meta-analysis *PLoS medicine*, 9(11), e1001349.
- O'Connor, M. F., Bower, J. E., Cho, H. J., Creswell, J. D. , Dimitrov, S. , Hamby, M. E., . . . Irwin, M. R. (2009). To assess, to control, to exclude: Effects of biobehavioral factors on circulating inflammatory markers. *Brain, Behavior, & Immunity*, 23(7), 887-897.
- O'Donovan, A., Slavich, G. M., Epel, E. S., & Neylan, T. C. (2012). Exaggerated neurobiological sensitivity to threat as a mechanism linking anxiety with increased risk for diseases of aging. *Neuroscience & Biobehavioral Reviews*, 37(1), 96-108.
- Oberleitner, L. M. S, Smith, P. H., Weinberger, A. H., Mazure, C. M., & McKee, S. A. (2015). Impact of exposure to childhood maltreatment on transitions to alcohol dependence in women and men. *Child Maltreatment*, 20(4), 301-308.
- Ong, A. D., Rothstein, J. D., & Uchino, B. N. (2012). Loneliness accentuates age differences in cardiovascular responses to social evaluative threat. *Psychology and Aging*, 27(1), 190.
- Oosterman, M., De Schipper, J C., Fisher, P. , Dozier, M., & Schuengel, C. (2010). Autonomic reactivity in relation to attachment and early adversity among foster children. *Development and Psychopathology*, 22(1), 109-118.
- Ouellet-Morin, I., Odgers, C. L., Danese, A., Bowes, L., Shakoor, S., Papadopoulos, A. S., . . . Arseneault, L. (2011). Blunted cortisol responses to stress signal social and behavioral

- problems among maltreated/bullied 12-year-old children. *Biological Psychiatry*, 70(11), 1016-1023.
- Pace, T., Mletzko, T., Alagbe, O., Musselman, D., Nemeroff, C. B., Miller, A., & Heim, C. (2006). Increased stress-induced inflammatory responses in male patients with major depression and increased early life stress. *American Journal of Psychiatry*, 163(9), 1630-1633.
- Paikoff, R. L., & Brooks-Gunn, J. (1991). Do parent-child relationships change during puberty? *Psychological Bulletin*, 110(1), 47-66.
- Park, H., Tsai, K. M., Dahl, R. E., Irwin, M.R., McCreath, H., Seeman, T. E., & Fuligni, A. J. (2016). Sleep and inflammation during adolescence. *Psychosomatic Medicine*, 78(6), 677-685.
- Pauletto, P., & Rattazzi, M. (2006). Inflammation and hypertension: the search for a link. *Nephrology Dialysis Transplantation*, 21(4), 850-853.
- Phillips, T. M., Wilmoth, J. D., Wall, S. K., Peterson, D. J., Buckley, R., & Phillips, L. E. (2013). Recollected parental care and fear of intimacy in emerging adults. *The Family Journal*, 21(3), 335-341.
- Poon, C. Y. M., & Knight, B. G. (2011). Impact of childhood parental abuse and neglect on sleep problems in old age. *Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, 66B(3), 307-310.
- Prather, A. A. , Marsland, A. L., Hall, M., Neumann, S. A., Muldoon, M. F., & Manuck, S. B. (2009). Normative variation in self-reported sleep quality and sleep debt is associated with stimulated pro-inflammatory cytokine production. *Biological Psychology*, 82(1), 12-17.

- 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(7), 916-931.
- Puterman, E., Epel, E.S., O'Donovan, A., Prather, A. A., Aschbacher, K., & Dhabhar, F. S. (2014). Anger is associated with increased IL-6 stress reactivity in women, but only among those low in social support. *International journal of behavioral medicine*, 21(6), 936-945.
- Radloff, L. S. (1977). The CES-D scale: A self-report depression scale for research in the general population. *Applied psychological measurement*, 1(3), 385-401.
- Raison, C. L., Capuron, L., & Miller, A. H. (2006). Cytokines sing the blues: inflammation and the pathogenesis of depression. *Trends in Immunology*, 27(1), 24-31.
- Raposa, E. B., Bower, J. E., Hammen, C. L., Najman, J. M., & Brennan, P. A. (2014). A developmental pathway from early life stress to inflammation: The role of negative health behaviors. *Psychological Science*, 25(6), 1268-1274.
- Redlich, R., Stacey, D., Opel, N., Grotegerd, D., Dohm, K., Kugel, H., . . . Dannlowski, U. (2015). Evidence of an IFN- $\gamma$  by early life stress interaction in the regulation of amygdala reactivity to emotional stimuli. *Psychoneuroendocrinology*, 62, 166-173.
- Repetti, R. L., Taylor, S. E., & Seeman, T. E. (2002). Risky families: Family social environments and the mental and physical health of offspring. *Psychological Bulletin*, 128(2), 330-366. doi: 10.1177/074355489272005
- 10.1037/0022-006X.64.1.8

- Rohleder, N. (2011). Variability in stress system regulatory control of inflammation: a critical factor mediating health effects of stress. *Expert Review of Endocrinology & Metabolism*, 6(2), 269-278.
- Rohleder, N. (2014). Stimulation of systemic low-grade inflammation by psychosocial stress. *Psychosomatic Medicine*, 76(3), 181-189.
- Roy, M. P., Steptoe, A., & Kirschbaum, C. (1998). Life events and social support as moderators of individual differences in cardiovascular and cortisol reactivity. *J Pers Soc Psychol*, 75(5), 1273-1281.
- Sansone, R. A., Edwards, H. C., & Forbis, J. S. (2010). The relationship Between caretaking experiences in childhood and sleep disturbances in adulthood. *Psychiatry (Edgmont)*, 7(5), 33.
- Schlotz, W., Hammerfald, K., Ehlert, U., & Gaab, J. (2011). Individual differences in the cortisol response to stress in young healthy men: Testing the roles of perceived stress reactivity and threat appraisal using multiphase latent growth curve modeling. *Biological Psychology*, 87(2), 257-264.
- Schreier, H. M. C., Roy, L. B., Frimer, L. T., & Chen, E. (2014). Family chaos and adolescent inflammatory profiles: The moderating role of socioeconomic status. *Psychosomatic Medicine*, 76(6), 460-467.
- Schwerdtfeger, A. R., & Schlagert, H. (2011). The conjoined effect of naturalistic perceived available support and enacted support on cardiovascular reactivity during a laboratory stressor. *Annals of Behavioral Medicine*, 42(1), 64-78.
- Seery, M. D. (2011). Resilience: a silver lining to experiencing adverse life events? *Current Directions in Psychological Science*, 20(6), 390-394.

- Shapero, B. G., Black, S.K., Liu, R.T., Klugman, J., Bender, R. E., Abramson, L. Y., & Alloy, L. B. (2014). Stressful life events and depression symptoms: the effect of childhood emotional abuse on stress reactivity. *Journal of clinical psychology*, 70(3), 209-223.
- Shearer, W. T., Reuben, J. M., Mullington, J. M. , Price, N. J., Lee, B. N., Smith, E. O. , . . . Dinges, D. F. (2001). Soluble TNF-alpha receptor 1 and IL-6 plasma levels in humans subjected to the sleep deprivation model of spaceflight. *Journal of Allergy and Clinical Immunology*, 107(1), 165-170.
- Shields, A., & Cicchetti, D. (1998). Reactive aggression among maltreated children: The contributions of attention and emotion dysregulation. *Journal of Clinical Child Psychology*, 27(4), 381-395.
- Sin, N. L., Sloan, R. P., McKinley, P. S., & Almeida, D. M. (2016). Linking daily stress processes and laboratory-based heart rate variability in a national sample of midlife and older adults. *Psychosomatic Medicine*, 78(5), 573-582.
- Sladek, M. R., & Doane, L. D. (2015). Daily diary reports of social connection, objective sleep, and the cortisol awakening response during adolescents' first year of college. *J Youth Adolesc*, 44(2), 298-316.
- Slopen, N., Koenen, K. C., & Kubzansky, L. D. (2012). Childhood adversity and immune and inflammatory biomarkers associated with cardiovascular risk in youth: a systematic review. *Brain, Behavior, & Immunity*, 26(239-250).
- Slopen, N., Kubzansky, L. D., McLaughlin, K. A., & Koenen, K. C. (2013). Childhood adversity and inflammatory processes in youth: A prospective study. *Psychoneuroendocrinology*, 38(2), 188-200.

- Slopen, N., Lewis, T. T., Gruenald, T. L., Mujahid, M. S., Ryff, C. D., Albert, M. A., & Williams, D. R. (2010). Early life adversity and inflammation in African Americans and Whites in the midlife in the United States Survey. *Psychosomatic Medicine*, 72, 694-701.
- Smetana, J. G., Campione-Barr, N., & Metzger, A. (2006). Adolescent development in interpersonal and societal contexts. *Annu Rev Psychol*, 57, 255-284.
- Somerville, L. H. (2013). The teenage brain: Sensitivity to social evaluation. *Current Directions in Psychological Science*, 22(2), 121-127.
- St Clair, M. C., Croudace, T., Dunn, V. J., Jones, P. B., Herbert, J., & Goodyer, I. M. (2015). Childhood adversity subtypes and depressive symptoms in early and late adolescence. *Development and Psychopathology*, 27(03), 885-899.
- Steptoe, A., Hamer, M., & Chida, Y. (2007). The effects of acute psychological stress on circulating inflammatory factors in humans: a review and meta-analysis. *Brain, Behavior, and Immunity*, 21(7), 901-912.
- Stetler, C. , & Miller, G. E. (2011). Depression and hypothalamic-pituitary-adrenal activation: A quantitative summary of four decades of research. *Psychosomatic Medicine*, 73(2), 114-126.
- Strahler, J., Mueller, A., Rosenlocher, F., Kirschbaum, C., & Rohleder, N. (2010). Salivary  $\alpha$ -amylase stress reactivity across different age groups. *Psychophysiology*, 47(3), 587-595.
- Strong, J. P., Malcom, G. T., McMahan, C. A., Tracy, R. E., Newman III, W. P., Herderick, E. E., & Cornhill, J. F. (1999). Prevalence and extent of atherosclerosis in adolescents and young adults: implications for prevention from the Pathobiological Determinants of Atherosclerosis in Youth Study. *Journal of the American Medical Association*, 281(8), 727-735.

- Stroud, L. R., Foster, E. , Papandonatos, G. D., Handwerger, K., Granger, D. A., Kivlighan, K. T., & Niaura, R. (2009). Stress response and the adolescent transition: Performance versus peer rejection stressors. *Development and Psychopathology*, 21(1), 47-68.
- Suarez, E. C. (2008). Self-reported symptoms of sleep disturbance and inflammation, coagulation, insulin resistance and psychosocial distress: Evidence for gender disparity. *Brain, Behavior, & Immunity*, 22(6), 960-968.
- Sullivan, M. W., Bennett, D. S., & Lewis, M. (2013). Individual differences in the cortisol responses of neglected and comparison children. *Child Maltreatment*, 18(1), 8-16.
- Tardy, C. H., Thompson, W. R., & Allen, M. T. (1989). Cardiovascular responses during speech: does social support mediate the effects of talking on blood pressure?'. *Journal of Language and Social Psychology*, 8(3-4), 271-285.
- Tataranni, P. A., Young, J. B., Bogardus, C., & Ravussin, E. (1997). A low sympathoadrenal activity is associated with body weight gain and development of central adiposity in Pima Indian men. *Obesity research*, 5(4), 341-347.
- Taylor, S. E., Karlamangla, A. S., Friedman, E. M., & Seeman, T. E. (2011). Early environment affects neuroendocrine regulation in adulthood. *Social Cognitive and Affective Neuroscience*, 6(2), 244-251.
- Taylor, S. E., Lehman, B. J., Kiefe, C. I., & Seeman, T. E. (2006). Relationship of early life stress and psychological functioning to adult C-reactive protein in the coronary artery risk development in young adults study. *Biological Psychiatry*, 60(8), 819-824.
- Taylor, S. E., Lerner, J. S., Sage, R. M., Lehman, B. J., & Seeman, T. E. (2004). Early environment, emotions, responses to stress, and health. *Journal of Personality*, 72(6), 1365-1394.

- Taylor, S. E., Sherman, D. K., Kim, H. S., Jarcho, J., Takagi, K., & Dunagan, M. S. (2004). Culture and social support: Who seeks it and why? *J Pers Soc Psychol*, 87(3), 354-362. doi: 10.1037/0022-3514.87.3.354
- Taylor, S. E., Welch, W. T., Kim, H. S., & Sherman, D. K. (2007). Cultural differences in the impact of social support on psychological and biological stress responses. *Psychological Science*, 18(9), 831-837.
- Taylor, Z. E., Spinrad, T. L., VanSchyndel, S. K., Eisenberg, N., Huynh, J., Sulik, M. J., & Granger, D. A. (2013). Sociodemographic risk, parenting, and effortful control: Relations to salivary alpha-amylase and cortisol in early childhood. *Developmental Psychobiology*, 55(8), 869-880.
- Teisl, M., & Cicchetti, D. (2008). Physical abuse, cognitive and emotional processes, and aggressive/disruptive behavior problems. *Social Development*, 17(1), 1-23.
- Thase, M. E. (2006). Depression and sleep: Pathophysiology and treatment. *Dialogues in Clinical Neuroscience*, 8(2), 217-226.
- Thoma, M. V., Kirschbaum, C., Wolf, J. M., & Rohleder, N. (2012). Acute stress responses in salivary alpha-amylase predict increases of plasma norepinephrine. *Biological Psychology*, 91(3), 342-348.
- Topitzes, J., Mersky, J. P., & Reynolds, A. J. (2009). Child maltreatment and adult cigarette smoking: A long-term developmental model. *Journal of Pediatric Psychology*, jsp119.
- Tottenham, N., Hare, T. A., Millner, A., Gilhooly, T., Zevin, J. D., & Casey, B. J. (2011). Elevated amygdala response to faces following early deprivation. *Developmental Science*, 14(2), 190-204. doi: 10.1111/j.1467-7687.2010.00971.x

- Tsai, K. M., Telzer, E. H., & Fuligni, A. J. (2013). Continuity and discontinuity in perceptions of family relationships from adolescence to young adulthood. *Child Development, 84*(2), 471-484.
- Turney, K. (2011). Labored love: Examining the link between maternal depression and parenting behaviors. *Social Science Research, 40*(1), 399-415.
- Uchino, B. N. (2006). Social support and health: a review of physiological processes potentially underlying links to disease outcomes. *Journal of Behavioral Medicine, 29*(4), 377-387.
- Uchino, B. N., Ruiz, J. M., Smith, T. W., Smyth, J. M., Taylor, D. J., Allison, M., & Ahn, C. (2016). Ethnic/racial differences in the association between social support and levels of C-reactive proteins in the North Texas Heart Study. *Psychophysiology, 53*(1), 64-70.
- Uhart, M., Chong, R. Y., Oswald, L., Lin, P., & Wand, G. S. (2006). Gender differences in hypothalamic–pituitary–adrenal (HPA) axis reactivity. *Psychoneuroendocrinology, 31*(5), 642-652.
- Umberson, D., Williams, K. D., Thomas, P. A., Liu, H., & Thomeer, M. Beth. (2014). Race, gender, and chains of disadvantage childhood adversity, social relationships, and health. *Journal of Health and Social Behavior, 55*(1), 20-38.
- Uno, D., Uchino, B. N., & Smith, T. W. (2002). Relationship quality moderates the effect of social support given by close friends on cardiovascular reactivity in women. *International journal of behavioral medicine, 9*(3), 243-262.
- van Harmelen, A. L., van Tol, M. J., Demenescu, L. R., van der Wee, N. J., Veltman, D. J., Aleman, A., . . . Elzinga, B. M. (2012). Enhanced amygdala reactivity to emotional faces in adults reporting childhood emotional maltreatment. *Social Cognitive and Affective Neuroscience*. doi: 10.1093/scan/nss007

- van Leeuwen, W. M. A., Lehto, M., Karisola, P., Lindholm, H., Luukkonen, R., Sallinen, M., . . . Alenius, H. (2009). Sleep restriction increases the risk of developing cardiovascular diseases by augmenting proinflammatory responses through IL-17 and CRP. *PLoS One*, 4(2), 1-7.
- Vgontzas, A. N., Zoumakis, E., Bixler, E. O., Lin, H. M., Follett, H., Kales, A., & Chrousos, G. P. (2004). Adverse effects of modest sleep restriction on sleepiness, performance, and inflammatory cytokines. *The Journal of Clinical Endocrinology & Metabolism*, 89(5), 2119-2126.
- Watson, D., & Clark, L. A. (1994). The PANAS-X: Manual for the Positive and Negative Affect Schedule-Expanded form. *Ames: University of Iowa*.
- Wellen, K. E., & Hotamisligil, G. S. (2005). Inflammation, stress, and diabetes. *Journal of Clinical Investigation*, 115(5), 1111-1119.
- Wickrama, K. A. S., Conger, R. D., Lorenz, F. O., & Jung, T. (2008). Family antecedents and consequences of trajectories of depressive symptoms from adolescence to young adulthood: A life course investigation. *Journal of Health and Social Behavior*, 49(4), 468-483.
- Wickrama, K. A. S., Conger, R. D., Wallace, L. E., & Elder Jr, G. H. (2003). Linking early social risks to impaired physical health during the transition to adulthood. *Journal of Health and Social Behavior*, 44(1), 61-74.
- Wirtz, P. H., von Känel, R., Emini, L., Suter, T., Fontana, A., & Ehlert, U. (2007). Variations in anticipatory cognitive stress appraisal and differential proinflammatory cytokine expression in response to acute stress. *Brain, Behavior, and Immunity*, 21(6), 851-859.

- Yang, J. H., Lee, E. O., Kim, S. E., Suh, Y. H., & Chong, Y. H. (2012). Norepinephrine differentially modulates the innate inflammatory response provoked by amyloid- $\beta$  peptide via action at  $\beta$ -adrenoceptors and activation of cAMP/PKA pathway in human THP-1 macrophages. *Experimental Neurology*, 236(2), 199-206.
- Yang, Y. C., McClintock, M. K., Kozloski, M., & Li, T. Y. (2013). Social Isolation and Adult Mortality The Role of Chronic Inflammation and Sex Differences. *Journal of Health and Social Behavior*, 54(2), 183-203.
- Yang, Y. C., Schorpp, K. , & Harris, K. M. (2014). Social support, social strain and inflammation: Evidence from a national longitudinal study of U.S. adults. *Social Science & Medicine*, 107, 124-135.
- Yee, B. W. K., DeBaryshe, B. D., Yuen, S., Kim, S. Y., & McDubbin, H. I. (2007). Asian American and Pacific Islander families: Resiliency and life-span socialization in a cultural context. In F. T. L. Leong, A. Ebreo, L. Kinoshita, A. G. Inman, L. H. Yang & M. Fu (Eds.), *Handbook of Asian American Psychology* (pp. 295-316). Thousand Oaks, CA: Sage Publications.
- Zagon, A., & Smith, A. D. (1993). Monosynaptic projections from the rostral ventrolateral medulla oblongata to identified sympathetic preganglionic neurons. *Neuroscience*, 54(3), 729-743.