CHILDHOOD ABUSE AND PHYSIOLOGICAL DYSREGULATION

IN MIDLIFE AND OLD AGE

by

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ABSTRACT OF THE DISSERTATION

Childhood Abuse and Physiological Dysregulation in Midlife and Old Age

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The overarching goal of my research is to incorporate sociological perspectives (the life course perspective, inequality theory) with biomedical knowledge (stress theory) to document midlife and old age health for victims of childhood abuse. Using data from the National Survey of Midlife Development in the U.S. (MIDUS), I explore the extent to which childhood abuse creates physiological dysregulation and chronic diseases: cortisol abnormality (Chapter 2), metabolic syndrome (MetS) (Chapter 3), elevated markers of inflammation (Chapter 4), and three immune-related disorders (asthma, allergies, arthritis) (Chapter 2). I then explore the extent to which these associations are explained by three potential mediators: behavioral risk factors (sleeping and eating problems, body mass index [BMI]), perceived stress, and social relationship quality (Chapters 3-4). I also investigate whether profiles of childhood abuse and the pathways linking abuse to MetS differ by gender (Chapter 3). Finally, I assess whether the effects of childhood abuse on inflammatory markers vary by age group (Chapter 4).

I find five distinct classes of childhood abuse for the full sample and for women and four for men. Women are more likely than men to report frequent emotional and sexual abuse. Childhood abuse is associated with low cortisol levels and immune-related disorders. Low levels of cortisol partially mediate the association between abuse and both allergies and arthritis. Some abuse subgroups are at greater risk of MetS than the no abuse subgroup. For women, frequent

sexual abuse increases the risk of MetS; this association is not statistically significant among men. The associations between abuse and inflammatory markers vary by age. In the younger age groups (ages 34-44 and 45-54), the levels of inflammatory markers for victims are higher than non-victims; there are no statistically significant differences in the older age groups (ages 55-64 and 65-84). Victims are at greater risk of mortality, suggesting that selective mortality might contribute to the reduced gap in the older age cohorts. High BMI, sleep problems, and weak or strained family ties partially mediate the association. Overall, my project demonstrates how integrating sociological perspectives and biomedical knowledge illuminates the associations between early life adversity and adult health consequences.

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and dad, I believe that you are always with me and are watching over me. Thank you for your endless support of this project. It was all for you!

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Chapter 1-Introduction

Incorporating Biology into Social Research on Health over the Life Course

During the past few decades, research examining biomedical perspectives on individuals'

social behaviors and attributes has increased dramatically. Studies find, for instance, that high

levels of testosterone are associated with smoking, multiple sexual partners (Booth et al. 1999),

and social dominance (Schaal et al. 1996). Maltreated children with certain genotypes (e.g., high

levels of monoamine oxidase A [MAOA]) are less likely to engage in antisocial behaviors than

their counterparts with other genotypes (low levels of MAOA) (Caspi et al. 2002). Some studies

even suggest that individuals seek out friends who have the same genetic variants that they do

(Fowler et al. 2011). Biomedical perspectives are therefore significantly influencing many areas

of sociology, such as gender (masculinity), criminology (delinquency and crime), and social

networks.

Likewise, sociological perspectives have improved our understanding of how social

environments shape the relationship between biology and behavior (Freese et al. 2003; Guo

2006). For example, there is a significant positive association between testosterone and antisocial

behavior, yet this effect is more pronounced for people with low SES than for those with high

SES (Dabbs et al. 1990). For women, education levels might moderate genetic reactivity to

postpartum depression (PPD)-like symptoms. Among women with the serotonin transporter gene,

those with a college degree are less likely than women without a college degree to report PPD-

like symptoms (Mitchell et al. 2011). Hence, social factors, if disregarded, might lead to biased

estimations of biological pathways in human behaviors (Freese 2006; Freese et al. 2003).

Regarding this trend, many sociologists, as compared to scholars in other disciplines,

have been reluctant to employ biomedical perspectives and biologically-informed data in their

research (Chaufan 2007). Possible reasons might include some sociologists' resistance to

biological determinism (i.e., "geneticization") or their lack of biomedical training. Increasing numbers of scholars working in biosociology, however, emphasize that fellow sociologists should devote more effort to reconciling their social theories or models (e.g., constructionist models of gender and social control) with prevailing theories or evidence in the biomedical sciences (Freese et al. 2003; Guo 2006; Udry 2000). Both sociology and biology would benefit from such integration.

Life course perspectives on health inequalities provide one compelling example of how sociological perspectives (e.g., cumulative inequality theory) can be integrated with biomedical findings and knowledge (e.g., theory of stress). For example, they can assist in efforts to better understand aging processes, the development of disease and disability, and death (Ferraro and Shippee 2009). The biological perspective (e.g., theory of stress) identifies the mechanisms involved in how stress, generated by social forces (e.g., social hierarchies and inequality), "gets under the skin," that is, alters physiological systems and increases the risk of developing diseases. Sociological perspectives suggest that the likelihood of an individual being exposed to stress varies by his or her social position, such as SES, gender, and race (Thoits 2010). Resilience factors (e.g., social support), which attenuate or buffer the stress effects on health outcomes, also vary by the individual's social position (Thoits 2010). Therefore, the association between stress and health outcomes will be more fully understood when both perspectives are taken into account.

Over the past decade, large population-based datasets have begun to include biomedical measures (biomarkers) (Hauser and Weir 2010; McDade et al. 2007). This trend allows sociologists to incorporate biomedical information in their research. There are three main reasons, I believe, why using biomarkers in population-based data helps sociologists more fully understand the social determinants of lifelong health. First, since biomarkers reflect both normative processes and pathogenic states of body systems (Piazza et al. 2010), the collection and use of biomarkers in population-based data has opened a new window on the study of health

across the life course. By using biomarkers, researchers can describe both aging and disease processes, which might be determined by certain physiological sequences: the dysregulation of body systems, the incidence of disease, the development of disease, and, ultimately, death (Crimmins et al. 2010; Lindau and McDade 2007).

Second, by taking biomarkers into account, researchers can compensate for limitations associated with the use of self-reported measures of health. While these measures provide information on conscious or cognitive experiences of health, biomarkers are objective measures of physical health representing a wide range of organ functions and physiological processes (McDade et al. 2007). Therefore, including both self-reported measures of health and biomarkers has statistical benefits (increasing explanatory power and reducing the chance of type I errors), thus allowing researchers to more accurately understand health outcomes (McDade 2008). Third and finally, whereas biomedical research typically studies small samples within clinical settings, the use of population-based data grants access to more variance in social variables, such as SES, gender, and race, which can provide useful insights for biomedical or clinical research.

Life Course Approaches to Studying Health Trajectories: Why Early Life Experiences are Important

Life course approaches to health, which integrate biological, cognitive, social, and behavioral mechanisms, suggest that an individual's early life experiences are precursors to later health outcomes (Kuh et al. 2003; Lupien et al. 2009). Of all the life course stages, childhood is one of the most important periods for generating an individual's health trajectory (Shonkoff et al. 2009). There are several reasons why childhood experiences play important roles in health outcomes across the life course.

Early childhood, especially infancy and toddlerhood, is a critical period when, though increasing complexity and adaptation, rapid changes occur in the organs, increasing the efficiency of the body's systems (Lupien 2009). During this period, exposure to toxic environments,

including extreme and repeated stressors, might have lifelong effects on the structure and function

of body systems (e.g., hypothalamic-pituitary-adrenal [HPA] axis activity and the secretion of

stress hormones). Such effects might not be modified in any dramatic way in later life (Ben-

Shlomo and Kuh 2002; de Bellis et al. 1994). A developmental model for disease (e.g.,

"biological programming"), introduced by Barker (1990; 1995), is an example of a critical period

model. The evidence shows that abnormal patterns of an individual's growth trajectory during

prenatal and postnatal periods affect the risk of developing coronary heart disease (CHD).

Individuals, for example, who grow slowly during fetal development, due to under- or mal-

nutrition during gestation, and then have accelerated weight gain in infancy and early childhood,

will have an elevated risk of CHD in adulthood (Barker 2002). In addition, the parts of the brain

that regulate the stress response (e.g., the hippocampus) have a greater degree of sensitivity and

plasticity during infancy and toddlerhood than at other stages of the life course (Lupien et al.

2009). Thus, stressors experienced during the first few years of life might affect physical and

mental health in direct and immediate ways, such as hippocampal damage (Glaser 2000), or have

an "incubation period," thus increasing their risk of developing diseases in adulthood (Miller et

al. 2009).

Childhood is a sensitive period when exposure to stress has a stronger effect on the risk

of developing disease than at other times in life; similar exposure to stress outside this sensitive

period may still increase the risk of disease and delay behavioral and cognitive development, but

this impact will be weaker than if it occurs during this sensitive period (Ben-Shlomo and Kuh

2002). According to attachment theory (Bowlby 1988), an infant or child develops an attachment

through interactions with the primary caregiver(s). Children construct internal working models of

self and parent(s), and these models help predict how others will treat them. Children who are

abused by a primary caregiver might not develop secure attachments throughout the life course

(Carlson et al. 1989). When children fail to build up secure attachments and psychological

strength, including trust and self-control, they may encounter difficulties in developing social skills (e.g., peer and romantic/sexual relationships) beyond childhood (Hazan and Shaver 1987).

In addition, research finds that there are neurobiological correlates associated with each pattern of attachment (Schore 2000). Infants who are securely attached to their primary caregiver are less likely to have brain alterations due to elevated stress hormones than infants with insecure attachments (Gunnar et al. 1996), while infants who are insecurely attached to their primary caregiver are more likely to have abnormal heart activity than infants with secure attachments (Izard et al. 1991). A secure attachment may even help decrease the risk of developing chronic diseases in adulthood. One study finds that among middle-aged individuals who grew up in poor households, those who were raised with a high level of maternal nurturance are less likely to develop MetS, compared to those who were raised with a low level of maternal nurturance (Miller et al. 2011b). These findings suggest that secure attachment and strong social ties can moderate poor health outcomes that stem from childhood adversities.

Moreover, experiencing adversities during childhood increases the likelihood of experiencing subsequent negative life events. Inequality theories underscore the importance of early life environments for subsequent life trajectories (Dannefer 2003; Ferraro and Shippee 2009; Pearlin et al. 2005). Similarly, according to "chain of risk" or "stress proliferation" models, once an individual encounters an adversity/stressor, individuals have a higher chance of encountering additional adversities/stressors (Ben-Shlomo and Kuh 2002; Pearlin et al. 2005; Rutter 1989) which in turn influence adult health. Moreover, an "accumulation of risk" perspective suggests that the frequency, duration, and severity of exposures might determine the likelihood of repairing damaged body systems (Kuh et al. 2003).

Many studies indicate that individuals who experience childhood abuse are more likely to experience additional adversities and develop psychological problems that carry long-term consequences for health, including antisocial traits (Schore 2003), poor academic and classroom performance (Zolotor et al. 1999), juvenile delinquency, criminal behavior and incarceration as

an adult (Maxfield and Widom 1996), unemployment (Currie and Widom 2010), and alcohol or other drug use (Lee et al. 2012). Cumulatively, these experiences could contribute to a high level of perceived distress and to low SES achievement, both of which increase the risk of developing chronic diseases in adulthood.

Stress and Physiological Systems

Stress. In a series of pioneering studies, Hans Selye (1956) developed the concept of stress and stressors by examining how various physical stressors (e.g., cold, heat, and infection) affect body systems. Since then, numerous studies have documented the association between stressors and various physiological responses, including sympathetic arousal (e.g., increased blood pressure), HPA axis activity, immune functions, and the release of stress hormones (e.g., catecholamines and cortisol).

Whereas Selye focused mainly on physiological stressors, psychologists, and other health scholars after him have been more interested in psychological stressors (Lovallo 2005), which have been conceptualized and categorized in numerous ways. Most stress researchers agree that the major psychological stressors fall into four broad categories: negative life events, lifetime traumatic events (childhood trauma and adulthood trauma), chronic stressors, and daily hassles (Almeida et al. 2011; Turner et al. 1995). Negative life events (e.g., divorce, job loss, or bankruptcy) indicate objectively reportable, observable, and discrete life changes; experiencing these kinds of events requires substantial adjustments in a person's life (Almeida et al. 2011; Turner et al. 1995; Wheaton 1997). A traumatic event (e.g., combat in war or sexual assault) can be a single/temporally isolated experience or a lasting/repeated event that might threaten an individual's health, safety, or survival, overwhelming their capacity to cope (Eisen and Goodman 1998; Glaser 2000). Chronic stressors are those which persist over an extended period of time, either through their continued presence in the environment or through their residual psychological effects. Caring for a spouse with Alzheimer's disease, for example, is a chronic stressor; a physical or sexual assault may be another example (Miller et al. 2007). Daily hassles are defined

as minor events that occur in the course of daily routines, such as spousal conflicts and work deadlines (Almeida et al. 2005).

Research suggests that the likelihood of being exposed to a stressor and its effects on health should be considered, based on the combinations of an individual's resilience and vulnerability to the stressor (Almeida et al. 2011). Moreover, the likelihood of exposure to stress and of having resilience varies by an individual's characteristics (race/ethnicity, gender, and SES), demonstrating that how social forces (e.g., social inequality) create adverse health outcomes (Thoits 2010). Therefore, individuals who grow up in poor environments are at greater risk of being exposed to multiple stressors, and their capacity to cope is typically low.

Physiological Systems in Response to Stress. Stressors disrupt the body's physiological regulatory processes. Recent studies have focused on how stress alters physiological systems and leads to the development of diseases in adulthood (Miller et al. 2009). Under stressful conditions, the body systems continue to respond to both internal and external challenges, adapt themselves to changing environmental stimuli, and try to achieve homeostasis, an optimized status of the body (Seeman et al. 1997). This dynamic physiological process of achieving homeostasis is defined as "allostasis" (Sterling and Eyer 1988). Yet, prolonged and/or repeated "wear and tear on the body" leads to allostatic load (AL) (McEwen 1998; Seeman et al. 2004; Seeman et al. 1997).

Stress involves a range of physiological systems, such as the HPA axis, the sympathetic-adrenal-medullary (SAM) axis, the neurotransmitter system, and the immune system (Glaser 2000). The HPA axis and the SAM axis are intensely studied areas related to psychological stress and the development of diseases (Cohen et al. 2007). Research also reveals the effects of stressor on immune alteration, which potentially influences the risk of developing autoimmune, inflammatory, and/or cardiovascular diseases (Irwin 2008). In the following sections, I briefly explain how these three systems respond to stress and contribute to the development of diseases.

The SAM System. The autonomic nervous system, consisting of the sympathetic nervous system and the parasympathetic nervous system, is a physiological system that immediately responds to stressful conditions. The catecholamines (epinephrine [EPI] and norepinephrine [NE]) are major stress hormones produced from the sympathetic neurons and the adrenal medulla under the control of the SAM system. These two hormones stimulate various organs (e.g., the salivary glands, lungs, and heart) and constrict blood vessels, helping the body to counteract stressors. Once an individual encounters stressors, EPI and NE are immediately released and help to decrease blood flow to the organs of the gastrointestinal tract, the skin, and the kidneys to maximize the blood flow and oxygen delivery to the brain, heart, and muscles. As a result, the individual can immediately counteract stressors through "fight-or-flight." Yet, continued activations of the SAM system, by prolonged and repeated stressors, can ultimately result in tissue damage and the dysregulation of the body (Lovallo 2005).

The function of the SAM system can be measured by various biomarkers (Crimmins and Seeman, 2001; Piazza et al, 2010). For example, NE, EPI, systolic and diastolic blood pressure, and heart rate are commonly used. Several studies indicate that individuals who experience chronic or high perceived stress display high levels of overnight urinary catecholamines (Kyoko et al. 2004) and increased heart rate and blood pressure (Matthews et al. 2004). Each of these physiological responses are related to adverse physical and cognitive functions (Seeman et al. 1997), the onset of cardiovascular diseases (Light et al. 1999), and an increased risk of mortality (Lewington et al. 2002).

The HPA axis. The HPA axis is another physiological pathway connecting the brain to the adrenal cortex, which secretes the stress hormone cortisol. Under stress stimuli, the hypothalamus releases the corticotrophin-releasing hormone (CRH) that in turn stimulates the anterior pituitary gland to secrete the adrenocorticotropic hormone (ACTH) into the bloodstream. When ACTH reaches the adrenal gland, it stimulates the adrenal cortex to produce and release cortisol into the blood. The secretion of cortisol is regulated by a negative feedback loop to

maintain an optimal level of cortisol. After the secretion of cortisol in response to stress, cortisol sends signals to reduce both the CRH and ACTH productions. In turn, they help decrease the secretion of cortisol (Chrousos 1995; Lovallo 2005). This negative feedback loop is considered as an internal balance mechanism in response to stressful conditions.

The stress hormone cortisol fulfills several functions, for example, suppressing the immune response as an anti-inflammatory hormone and increasing the levels of circulating glucose and energy storage (Chrousos and Gold 1992; Dickerson and Kemeny 2004). The functions of the HPA axis are measured by several biomarkers, such as CRH, ACTH, and cortisol. Studies indicate that prolonged and repeated activations of the HPA axis are related to abnormalities in the negative feedback loop and abnormal levels of the HPA axis biomarkers. Specifically, stress-induced HPA axis dysfunction and abnormal cortisol levels can be displayed by three different forms: hypercortisolism, hypocortisolism, and some forms of diurnal dysrhythmia (Adam and Gunnar 2001; Fries et al. 2005; Guilliams and Edwards 2010; Sapolsky et al. 1986).

Regarding these inconclusive findings related to abnormality of cortisol levels, Miller et al. (2007) propose that the timing of a stressor's onset might be a critical element in understanding the different forms of HPA axis dysfunction. That is, recent and ongoing stress is associated with increased HPA activity, while distant trauma is associated with decreased HPA activity. Research indicates that a dysregulation of the HPA axis is associated with several outcomes: problems related to memory, learning, and attention (Sapolsky 1996), psychological disorders (Sapolsky 2000), immunity disorders, and elevated markers of inflammation (Segerstrom and Miller 2004).

The Immune System. Like the SAM and the HPA axes, the immune system protects the body from various internal and external stimuli by destroying pathogens and preventing infection. Broadly, immune function entails two subsequent processes. One is an innate or non-specific immunity, and the other is an adaptive or specific immunity. Innate immunity is identified as a

primary defense system against infection. Once pathogens invade the body, immune cells, and proteins (e.g., natural killer cells, phagocytes, and complements) are immediately recruited to the sites of invasion through the production of cytokines (i.e., specialized chemical messengers). In addition, these immune cells and proteins also activate the immune system by cytokine communication. This adaptive immunity generates antigen-specific immunity by developing lymphocytes (e.g., T-lymphocytes and B- lymphocytes) with a high degree of specificity and "memory" against certain types of pathogens (Piazza et al. 2010; Segerstrom and Miller 2004).

Cytokines (e.g., interleukin [IL]-6, IL-10, and interferon-gamma) are involved in various functions of immunity: the development, maturation, and activation of immune system cells (Lovallo 2005). Amongst the various cytokines, IL-6 is a well-known inflammatory cytokine that is secreted by T-helper cells and macrophages. It leads to inflammation, a series of body protective processes, to fight against the invasion of viruses or bacteria. C-reactive protein (CRP) and fibrinogen are molecules produced in the liver in response to IL-6 (Friedman and Herd 2010). Like IL-6, high levels of CRP and fibrinogen are clinical signals of elevated risk of inflammation in the body (Danesh et al. 1998). Although the inflammation process is needed to protect the body from pathogens, without regulation, massive amounts of inflammatory cytokines are secreted and begin to damage healthy tissues (Lovallo 2005). Elevated levels of IL-6, CRP, or fibrinogen are associated with the risk of developing cardiovascular diseases and an increased risk of mortality (Danesh et al. 1998; Harris et al. 1999).

Psychological stressors, in particular traumatic and/or chronic stressors, can alter the immune system. Studies find that prolonged stress (e.g., long-term caregiving) significantly affects the levels of the immune/inflammatory biomarkers. Exposure to chronic stress, for instance, is associated with increased IL-6 (Kang and Fox 2001), weaker vaccine response (Glaser et al. 1992; Kiecolt-Glaser et al. 1996), and delayed wound healing (Marucha et al. 1998). In the following sections, I will discuss how one particular early life stressor, childhood abuse, alters physiological systems and increases the risk of developing chronic diseases in adulthood.

Childhood Abuse and Physiological Dysregulation

   Prevalence and Nature of Childhood Maltreatment. Childhood maltreatment causes immediate or latent harm to victims and includes all types of physical, emotional, and sexual abuse, as well as neglect and exploitation (World Health Oranization). Some research considers the regular experience of physical abuse as childhood trauma (Turner and Lloyd 1995). Some types of childhood maltreatment, such as sexual abuse, are regarded as major traumatic experiences which might have long-lasting cognitive and emotional consequences (Baum et al. 1993), while other types of maltreatment (e.g., educational neglect) might not be directly harmful but might have a negative effect on the victims (e.g., low SES achievement). Cicchetti and Toth (1993) suggest that the nature and consequences of childhood abuse and neglect depend on other characteristics of the abuse including the developmental period in which it occurred, it's chronicity/frequency, severity, and subtype, separations/placements, and the relationship of the abused to the abuser.

   According to official data from the National Child Abuse and Neglect Data System (NCANDS), from 2005 to 2009 the rates of unique victimization decreased from 10.9 to 9.3 children per 1000, yet still significant numbers of children become victims of childhood maltreatment (U.S. Department of Health and Human Services [USDHHS] 2010). An estimated 702,000 children, for example, were determined to be victims of child abuse and neglect in 2009 across all states. A nationally estimated 1,770 children died directly due to such abuse and neglect. The average age of the victims was around 6 years old, and one third of the victims were 3 years old or younger. Victims in the age group of birth to 1 year had the highest rate of victimization at 20.6 per 1,000 children. Data from NCANDS show that the victims experienced multiple types of maltreatment: neglect (78.3%) was the most common, followed by physical abuse (17.8%), sexual abuse (9.5%) and emotional abuse (7.6%). The overall rates of victimization were similar for boys (48.2%) and girls (51.1%) (USDHHS, 2010). Child characteristics, such as age, gender, and disability, affect the individual's vulnerability to

particular forms of abuse. For example, findings from both official data and self-reports of childhood maltreatment consistently show that girls are more likely than boys to experience sexual abuse (Dube et al. 2005; Sedlak et al. 2010; Thompson et al. 2004).

Consequences of Childhood Maltreatment over the Life Course. Research documents the impact of childhood abuse and neglect on an individual's developmental and health problems over the life course (Child Welfare Information Gateway 2008). For example, depression, anxiety, eating disorders, and suicidal ideation are common in young adulthood for those who experienced childhood maltreatment (Silverman et al. 1996). Victims of childhood abuse and neglect are also involved in various behavioral and social problems, including difficulties in peer relationships and low self-esteem in childhood (Bolger et al. 1998; Rogosch et al. 1995), substance use in both adolescence and adulthood (Dube et al. 2003), juvenile delinquency, and adult crime (Maxfield and Widom 1996). Victims of childhood abuse and neglect also suffer various medical illnesses throughout their lives, such as autoimmune disorders and cardiovascular diseases (Dube et al. 2009; Felitti et al. 1998; Springer et al. 2007). Research indicates that victims are more likely than non-victims to have cognitive, language, and academic deficits in childhood (Watts-English et al. 2006), which result in low SES in adulthood (Currie and Widom 2010). Having low SES might further influence the effects of childhood abuse on health consequences in adulthood.

Physiological Dysregulation in Response to Childhood Abuse

Abnormal HPA Axis Activities in Response to Childhood Abuse. The function of the HPA axis is a well-developed research area in studying childhood abuse and physiological dysregulation. The HPA system is not fully mature at birth. There are significant developmental changes throughout infancy and toddlerhood in the HPA axis (Lupien et al. 2009). Studies find that childhood maltreatment is associated with abnormal HPA axis activities and cortisol release, producing three forms of cortisol abnormality: hypercortisolism, hypocortisolism, and diurnal dysrhythmia of cortisol. Some research finds that abused children, compared to non-abused

children, exhibit a hyper-activation of the HPA axis, showing elevated secretion of cortisol (hypercortisolism) (Cicchetti and Rogosch 2001), yet other research finds that adults who were sexually abused as children or adolescents exhibit hypo-activation of the HPA axis, showing low cortisol levels (hypocortisolism) during young adulthood (Trickett et al. 2010). In addition, Taylor et al. (2011a) find that a lack of parental affection in childhood is associated with flat diurnal cortisol rhythms, a type of diurnal dysrhythmia of cortisol at midlife.

Regarding these mixed findings, a new wave of theories proposes a novel definition of cortisol regulation and its pathological effects (Fries et al. 2005; Raison and Miller 2003). These scholars have asserted that cortisol deviations in two directions, hypocortisolism and hypercortisolism, are detrimental and can trigger stress-related diseases (Heim et al. 2000a). For example, while an increased activation of the HPA axis is associated with melancholic depression, anorexia nervosa, and obsessive-compulsive disorders, a decreased activity of the HPA axis is associated with chronic fatigue syndrome, fibromyalgia, rheumatoid arthritis, asthma, and chronic pelvic pain (Fries et al. 2005; Guilliams and Edwards 2010). Since cortisol, like corticosteroids, is an anti-inflammatory agent, abnormal cortisol levels, particularly hypocortisolism, can lead to immune dysfunction and to elevated risk of inflammation (Fries et al. 2005), which might eventually increase the risk of developing immune system-related diseases.

Cardiovascular and Metabolic Systems Burdened in Response to Childhood Abuse. Childhood abuse is associated with the dysregulation of cardiovascular and metabolic systems that might in part originate from the overloaded activation of the SAM axis in response to stressors. For example, middle-aged adults who reported a history of physical abuse have an elevated risk of high blood pressure, circulation problems, and heart trouble (Springer et al. 2007). Multiple studies document that childhood abuse is associated with elevated levels of BMI in adulthood (Bentley and Widom 2009; Noll et al. 2007). Childhood abuse also increases the risk of developing multiple components of metabolic syndrome, such as elevated blood pressure, high

total cholesterol, raised glycosylated hemoglobin, and being overweight, in both young adulthood (Danese et al. 2009) and midlife (Thomas et al. 2008). Findings from these studies demonstrate the important role of childhood abuse in the development of diseases through the dysregulation of cardiovascular and metabolic systems.

Immune System Changes in Response to Childhood Abuse. Emerging studies indicate that early life adversities are associated with elevated levels of single and/or multiple inflammatory markers in adulthood, including IL-6, CRP, and fibrinogen. Childhood abuse and neglect are significantly associated with increased levels of CRP and fibrinogen (Danese et al. 2009). Low SES and poor family environments in childhood (e.g., childhood abuse and living with a substance abuser) are significantly related to elevated CRP (Taylor et al. 2006). Exposure to multiple life stressors during childhood and adolescence appears to be related to elevated single and/or multiple inflammatory markers: IL-6, CRP, and fibrinogen (Slopen et al. 2010). Slopen et al. (2010) indicate that a cumulative number of later negative life events (e.g., job loss, the loss of a child, or bankruptcy) and unhealthy conditions (e.g., high BMI) in adulthood might contribute to some parts of the association between childhood abuse and elevated markers of inflammation.

Limitations of Prior Studies

Despite important findings in recent studies, three major issues have been left unaddressed. First, prior studies have paid little attention to understanding the nature and context of childhood abuse and its association with physiological dysregulation. Often, the victims of childhood abuse experience multiple subtypes of abuse, each to a varying degree (Cicchetti and Toth 1993), yet many studies focus on only one type of abuse or use a narrow set of measures for childhood abuse. The prevalence of certain types of childhood abuse differs by gender, yet prior studies have paid little attention to the role of gender in comprehending the effects of childhood abuse on physiological dysregulation. Hence, it is necessary to investigate the extent to which gender explains variation in diverse profiles of childhood abuse and to test how each profile differently affects physiological dysregulation.

Second, most studies have considered psychosocial and behavioral factors (e.g., health behaviors and coping skills) as potential mediators between childhood abuse and physiological dysregulation, but these studies have overlooked testing the extent to which psychosocial and behavioral pathways link childhood abuse to physiological dysregulation. Given the well-established associations between childhood abuse and these factors, further research is needed to test these mediators, which ultimately will be useful for public health interventions to reduce adverse health outcomes for victims. In addition, although numerous clinical studies have examined the associations between childhood abuse and physiological dysregulation in adulthood, very few clinical studies and no population-based studies have tested the extent to which physiological dysregulation explains the associations between childhood abuse and stress-related diseases.

Third, aging plays a key role in physiological dysregulation (Almeida et al. 2011). Yet, few studies have investigated the associations between childhood abuse and physiological dysregulation beyond young adulthood, and to my knowledge, no study has tested how the associations vary over the life course. Selective mortality and "age-as-leveler" theories suggest that the effects of SES on health vary by stage of life course (House et al. 2005). As individuals age, differences in SES-based health disparities get smaller. This attenuation may reflect premature death among individuals with low SES or biological fragility among old people regardless of their SES. Selective mortality might vary by age, given the low SES that the victims of childhood abuse are likely to have in adulthood (Currie and Widom 2010). However, much of the research has failed to consider how selective mortality theory helps to account for age variations in the physiological outcomes of childhood abuse.

Aims and Outline of the Dissertation

My dissertation addresses five aims. First, using latent class analysis (an advanced method to help identify the heterogeneity of childhood abuse experiences), I will identify distinct profiles of childhood abuse that reflect a combination of frequency and subtype of abuse. Then I

will investigate whether these profiles of childhood abuse differ by gender. In the following two chapters (Chapters 2 and 3), I present my findings.

In Chapter 2 ("The Long-Term Effects of Childhood Abuse on Immune-Related Disorders at Midlife: Are Effects Explained by Low or High Cortisol Levels? "), I will investigate how childhood abuse leads to immune-related disorders, potentially mediated by extremely high or low levels of the stress hormone cortisol, due to abnormal activity of the HPA axis. Based on a new wave of theories related to bidirectional cortisol abnormality (Fries et al. 2005), I am particularly interested in testing the extent to which two different extremes in cortisol deviations (hypo- and hyper-cortisol levels) link childhood abuse to immune-related disorders (asthma, allergies, and arthritis).

In Chapter 3 ("Childhood Abuse and Metabolic Syndrome in Men and Women in Midlife: Poor Sleep Quality and Stress-Induced Eating as Potential Mechanisms"), I investigate associations between childhood abuse and metabolic syndrome (MetS), which is a combination of metabolic disturbances, including abdominal obesity, glucose intolerance, high blood pressure, and high bad and low good cholesterol levels (Alberti et al. 2006). The presence of MetS indicates an abnormal functioning of the cardiovascular and metabolic systems. Research indicates that there are gender differences in the nature of childhood abuse, in coping strategies in response to stress, and in the prevalence of MetS. Thus, I examine the associations between childhood abuse and MetS in men and women in midlife and the degree to which these associations are mediated by two psychosocial and behavioral pathways: poor sleep quality and stress-induced eating.

Chapter 4 ("Childhood Abuse and Elevated Markers of Inflammation in Adulthood: Do the Effects Differ across Life Course Stages?") addresses the associations between childhood abuse and the functioning of the immune system, as measured by inflammatory biomarkers. Guided by the life course perspective and selective mortality theory, I test whether childhood abuse affects inflammation levels in adulthood and whether the effect of childhood abuse on

elevated markers of inflammation varies across age groups. Moreover, I evaluate the extent to which these associations are mediated by four plausible pathways: sleep quality, BMI, perceived stress, and family social ties. Finally, in Chapter 5, I review my major findings, and I conclude by discussing limitations of this study, some directions for future research, the benefits and limitations of using biomarkers, and the implications of this study for policies and practices.

My dissertation makes several methodological and conceptual contributions to both sociological and biomedical research: 1) it provides a comprehensive history of childhood abuse using LCA; 2) it reveals the effects of childhood abuse on physiological dysregulation in multiple body systems (the HPA axis, the SAM axis, and the immune system); 3) it uses a cutting-edge biomedical theory (bidirectional cortisol abnormality) to explore the associations between childhood abuse and immune-related disorders; 4) it uncovers the important roles that gender and life course stages play in understanding the associations between childhood abuse and physiological dysregulation; and 5) it determines the extent to which health-risk or health-promoting behaviors explain the associations between childhood abuse and physiological dysregulation. Overall, my project demonstrates how sociological perspectives can be well integrated with biomedical knowledge to better understand the effects of early life adversities on health outcomes across the life course.

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Chapter 2-The Long-Term Effects of Childhood Abuse on Immune-Related Disorders in Midlife: Are Effects Explained by Low or High Cortisol Levels?

Abstract

The current study investigates the extent to which associations between childhood abuse and three immune-related disorders at midlife are mediated by extremely high or low levels of cortisol. Data come from the Biomarker study of the National Survey of Midlife Development in the United States (n = 898, aged 40 to 65 years). Based on prior studies, I define extremely high cortisol levels as those falling within the upper quartile and extremely low levels as those falling within the lower quartile. I examine three immune-related disorders as outcomes: asthma, arthritis, and allergies. Using latent class analysis (LCA), I identify five distinct profiles of childhood abuse, each reflecting a unique combination of the type of abuse and the frequency of each type: 1) no abuse (66%); 2) low emotional, no physical/sexual abuse (17%); 3) no emotional, no physical, and high sexual abuse (6%); 4) high emotional/physical, low sexual abuse (5%); and 5) high emotional/physical/sexual abuse (6%). I test the extent to which high or low cortisol levels explain the associations between these latent classes of childhood abuse and the three immune-related disorders. I find that victims of childhood abuse are more likely to have all three immune-related disorders, relative to non-victims. Individuals in groups that include high sexual abuse are more likely to have arthritis than those who are in less sexually abused groups. Compared to non-victims of childhood abuse, victims of childhood abuse are more likely to have low cortisol levels. Particularly, individuals who experienced high physical/emotional/sexual abuse have significantly lower cortisol levels than non-victims, even after accounting for all confounders. Individuals with low cortisol levels are more likely to have all three immune-related disorders, while those who have high cortisol levels are less likely to have these disorders. Low

cortisol levels help explain the associations between high childhood abuse and both allergies and arthritis. Yet, both childhood abuse and low levels of cortisol remain significant predictors of these disorders. Overall, the findings suggest extremely low levels of cortisol might partially explain why victims of childhood abuse are more likely to develop allergies and arthritis.

Keywords

stress; childhood abuse; cortisol; asthma; allergies; arthritis

Introduction

According to the life course perspective, individuals' early life experiences are precursors to health outcomes throughout their lives, and such experiences affect health through biological, cognitive, emotional, social, and behavioral pathways (Kuh et al. 2003; Lupien et al. 2009). Many studies have demonstrated that victims of childhood abuse have various mental and physical health problems over the life course (Felitti et al. 1998; Goodwin and Stein 2004). Studies have focused on psychosocial and behavioral pathways that link childhood abuse to adverse health consequences (Lee and White 2012; Springer 2009), yet few population-based studies have investigated the extent to which biological mechanisms explain why victims of childhood abuse, compared to non-victims, are at greater risk of developing chronic diseases.

Theories of stress and health have focused stress hormone abnormalities as a potential explanatory mechanism which links psychological stressors to stress-induced health conditions. Once a stressor is perceived by the cerebral cortex, the hypothalamic pituitary adrenal (HPA) axis (a major part of the neuroendocrine system's response to stress) is activated, releasing three stress hormones successively: the corticotropin-releasing hormone (CRH), the adrenocorticotropin hormone (ACTH), and cortisol (Lovallo 2005; Piazza et al. 2010). Cortisol is one of the most widely studied neuroendocrine hormones and is involved in several body systems: learning, memory function, and emotional response in the central nervous system; glucose storage and utilization in the metabolic system; and inflammatory response and the maturation of lymphocytes in the immune system (Miller et al. 2007; Sapolsky et al. 2000). In the short-term, cortisol helps the body release glucose and fatty acids, which provide energy to fight against stressors. It signals the brain to produce endorphins and suppresses the production and activation of proinflammatory cytokines. In the long-term, however, prolonged activation of the HPA axis results in abnormal patterns of cortisol secretion and eventually leads to deleterious health consequences, such as immune deficiency, cognitive impairment, inhibited growth, and hippocampal damage (Flinn and England 1997; Raison and Miller 2003). Since cortisol is one of

the well-known anti-inflammatory hormones that suppress the production and activation of proinflammatory cytokines, secreting abnormal levels of cortisol for an extended period of time might eventually lead to vulnerability to immune-related disorders (Heim et al. 2000a).

Several studies suggest that victims of childhood abuse are more likely than non-victims to exhibit abnormal secretion of cortisol. There are three different forms: 1) hypercortisolism (high levels of cortisol), 2) hypocortisolism (low levels of cortisol), and 3) diurnal dysrhythmia of cortisol (flat diurnal cortisol rhythms) (Cicchetti and Rogosch 2001; Taylor et al. 2011b; Trickett et al. 2010). Research demonstrates that chronically low or high cortisol output is detrimental and can trigger stress-related conditions, such as psychological disorders, immunity disorders, or problems related to learning and memory (Sapolsky 1996; Sapolsky 2000; Segerstrom and Miller 2004).

Most studies that have explored the associations between childhood abuse and cortisol levels in adulthood are limited to small samples collected from clinical settings, mostly consisting of women with a history of sexual abuse (Stein et al. 1997). In addition, many prior studies have used either an excessively narrow or excessively broad definition of childhood abuse, which may not capture the multifaceted subtypes of abuse or their severity, chronicity, or frequency (Cicchetti and Toth 1993; Irving and Ferraro 2006). Furthermore, I know of no study that examines abnormal secretion of cortisol as a potential mechanism linking childhood abuse and immune-related disorders. Using 898 middle-aged adults from the National Survey of Midlife Development in the U.S. (MIDUS), I examine the extent to which extreme cortisol levels explain the association between childhood abuse and three immune-related disorders: allergies, asthma, and arthritis.

Background

Childhood Abuse and Abnormal Secretion of Cortisol

Most previous theories about the stress response system have emphasized the role of increased cortisol levels on adverse health outcomes (Sapolsky et al. 1986). A new wave of theories, however, has re-conceptualized abnormal cortisol secretion as both extremely high (hypercortisolism) and extremely low (hypocortisolism), both of which may be detrimental and can trigger stress-related disease (Fries et al. 2005; Heim et al. 2000a; Raison and Miller 2003). For example, while hypercortisolism is associated with melancholic depression, anorexia nervosa, and obsessive-compulsive disorders, hypocortisolism is associated with chronic fatigue syndrome, fibromyalgia, rheumatoid arthritis, and asthma (Fries et al. 2005; Guilliams and Edwards 2010).

Miller and colleagues (2007) perform a meta-analysis of the association between different types of stressors and cortisol levels to provide information about these different forms of cortisol secretion. They find that abnormal secretion of cortisol is associated with the presence of stressors and that whether cortisol levels are high or low depends on both the nature of the stressor and when an individual experiences it. That is, recently experienced stressors (including continuing exposure) are associated with high levels of cortisol, while distant or traumatic stressors are associated with normalized or low levels of cortisol. Recent studies of childhood abuse and cortisol levels have also found either hypo- or hyper-activity in the HPA axis of those who were abused. The experience of childhood abuse is related to abnormal cortisol levels, and the degree of HPA activity might be determined by the temporal distance from the experience of abuse. One study finds that abused children (average 9.25 years of age) have higher levels of morning cortisol than non-abused children (Cicchetti and Rogosch 2001), but young women in their 20s who were sexually abused as children (the median age of abuse onset was 7.8 years) have lower morning cortisol levels than adults who were not abused (Trickett et al. 2010).

One possible mechanism responsible for hypocortisolism among adults who were victims of child abuse, compared to non-victims, may be that the HPA axis becomes prone to "down-regulate," that is, to overcompensate in response to prolonged hyper-activation by releasing

chronically low levels of cortisol (Heim et al. 2000b). Animal studies show that hypocortisolism occurs after a prolonged period of hyperactivity of the HPA axis due to chronic stress (Gómez et al. 1996). These findings are consistent with those based on human subjects. Using long-term prospective data from childhood to young adulthood (from age 6 to age 30), Trickett et al. (2010) find that women with a history of sexual abuse as children, compared to non-abused women, are more likely to have low morning cortisol levels from adolescence to early adulthood. As additional empirical evidence, van der Vegt et al. (2009) find that adoptees that experienced childhood abuse before their adoptions exhibit decreased levels of morning cortisol in adulthood, compared to those who were not abused. Moreover, Taylor et al. (2011a) find that individuals who received low levels of parental affection in childhood are more likely to show flat diurnal cortisol rhythms in midlife than those who received moderate levels of such affection. These findings implicate the role of early-life stressors in altering the HPA axis, which might eventually lead individuals to develop stress-induced diseases in adulthood.

Given the association between the timing of childhood abuse and reduced cortisol output, it is also reasonable to expect that cortisol secretion might be affected by the nature of childhood abuse, including its severity, frequency, or subtype (physical, emotional, or sexual). According to "chain of risk" or stress proliferation models, once an individual encounters a stressor, he or she has a higher chance of encountering secondary stressors (Ben-Shlomo and Kuh 2002; Pearlin et al. 2005). Hence, victims of childhood abuse might be more likely to experience subsequent stressors which in turn lead to abnormal levels of cortisol. To date, only limited evidence exists regarding the associations between different profiles of childhood abuse and the development of abnormal cortisol secretion. Most evidence supports the association between sexual abuse and hypocortisolism for women (Trickett et al. 2010), and a recent study shows that severe childhood neglect might be associated with hypocortisolism (van der Vegt et al. 2009). However, I know of no population-based studies that have investigated the extent to which different profiles of

childhood abuse are associated with the risk of releasing abnormal cortisol in adulthood. It is important to investigate this association.

Hypocortisolism and Stress-Related Disorders

Studies indicate that individuals who experience an early life stressor, such as childhood abuse, have an elevated risk of developing immune or inflammation-related disorders. Children who experience maltreatment are more likely to develop severe asthma than those who do not experience it (Lanier et al. 2010), and those who are physically abused as children are at greater risk of developing osteoarthritis (the most prevalent type of arthritis) than those who are not (Fuller-Thomson et al. 2009; Helmick et al. 2008). Similarly, population-based studies show that compared to non-victims, adults who were victims of physical abuse as children have an increased risk of arthritis, and victims of childhood neglect are more likely to have autoimmune disorders (Goodwin and Stein 2004). Another population-based study reports that compared to non-victims, adults who were victims of childhood abuse are more likely to be hospitalized due to autoimmune disorders (Dube et al. 2009).

If this is so, how does childhood abuse affect the development of these immune-related disorders? Raison and Miller (2003) suggest possible underlying biological mechanisms. They assert that abnormal cortisol secretion, particularly hypocortisolism, might play a major role in developing immune-related disorders. To be specific, both chronic and traumatic stress can cause "down-regulation" of the HPA axis and "insufficient glucocorticoid signaling," which in turn alter immunological functioning. Furthermore, cortisol is one of the most important anti-inflammatory hormones. That is, cortisol helps suppress the production and activation of proinflammatory cytokines, such as Interleukin (IL)-1, IL-6, and tumor necrosis factor alpha (TNF alpha). It helps constrain the inflammatory reaction and prevent tissue damage (Fries et al. 2005; Glaser and Kiecolt-Glaser 2005). However, a lack of cortisol results in unregulated immune functions, such as significantly increased inflammatory responses, which damage healthy tissue (Lovallo 2005).

Causal pathways between hypocortisolism and stress-related disorders are supported by animal studies, showing that a deficiency of corticosterone (i.e., cortisol for animals) in response to chronic stress causes arthritis (Gómez et al. 1996; Moncek et al. 2001; Sternberg et al. 1989). Human studies also provide suggestive evidence of an association between stress and immune functioning. Individuals who experience severe and chronic stress (e.g., long-term caregivers for individuals with cancer or Alzheimer's disease), for example, exhibit diminished sensitivity to glucocorticoids and have an elevated production of pro-inflammatory cytokines (for a review, see Segerstrom and Miller 2004). Accordingly, prolonged cortisol deficiency may lead to pathological immune functions, resulting in an increased risk of developing immune-related disorders. In particular, abused children might develop abnormal cortisol secretion and immune-related disorders in adulthood. Given the positive association between intensity of stress and negative health consequences (Lee et al. 2003), different profiles of childhood abuse might lead to different levels of cortisol, which in turn might play an important role in the development of immune-related disorders in adulthood.

The current study extends previous research by examining the associations among childhood abuse, abnormal cortisol secretion, and immune-related disorders. To my knowledge, this is the first study to examine the effects of abuse in childhood on stress-related disorders as potentially mediated by cortisol. Using a population-based survey, I address three research questions: 1) if an individual experiences childhood abuse, do they have an increased risk of developing immune-related disorders?; 2) are different profiles of childhood abuse associated with different levels of risk of developing immune-related disorders?; and 3) does secretion of very high or low levels of cortisol (hypercortisolism and hypercortisolism) explain the association between childhood abuse and immune-related disorders?

Data and Methods

Sample

The analytic sample comes from two subsamples of the Midlife Development in the United States (MIDUS) biomarker study: one from the respondents who participated in both the MIDUS I (1995-1996) and MIDUS II (2004-2005) surveys, and the other from a supplementary sample of African Americans from Milwaukee, Wisconsin (2004-2005), called the Milwaukee sample. The data for the biomarker study came from a two-day data-collection protocol at the General Clinical Research Center (GCRC). The data were collected between 2004 and 2009. Participants stayed overnight at the GCRC and completed the protocol with a clinician. This special module includes diverse biomarkers and detailed medical history as well as more comprehensive questions regarding childhood abuse than those in MIDUS I. The data collection for MIDUS was approved by the Health Sciences Institutional Review Board at the University of Wisconsin-Madison. I limit analytic sample to 898 middle-aged adults (ages 40-65) to reduce the large variations in HPA axis activity over the life course since older adults, compared to young adults, display higher ACTH and cortisol levels and impaired diurnal cycles of cortisol (Almeida et al. 2009; Kudielka et al. 2004).

MIDUS is a national study of health and aging among U.S. residents, aged 25 to 74 (b. 1920-1970), who were first interviewed between 1995 and 1996 (n = 7,108). The baseline study included a national sample, which was obtained through random digit dialing (RDD), and consists of respondents, siblings of many respondents (13% of the MIDUS I sample), and a national sample of twins (24% of the MIDUS I sample) of the same age range as the national RDD sample. Respondents were limited to only English speaking, non-institutionalized adults. A longitudinal follow-up of the MIDUS sample was conducted 10 years after the baseline assessment (2004-2005). At that point, a supplemental sample of 592 African Americans from Milwaukee, Wisconsin (Milwaukee sample) was recruited in order to investigate health in a highly segregated U.S. city. MIDUS II assessed a wide array of psychological constructs and demographic characteristics as well as extensive health measures. Based on the primary survey, four additional projects (Daily Diary Study, Cognitive Function, Bioindicators, and

Neuroscience) were conducted to explore the biopsychosocial pathways to various health

outcomes (Love et al. 2010).

Of those who initially responded to the questions in MIDUS I, 70% were interviewed in

MIDUS II, and 21% of MIDUS II sample (n = 1,054) and 39% of Milwaukee sample (n = 201)

attended the clinical examination, resulting in a total of 1,255 respondents. Compared to the

respondents in the primary national sample (MIDUS I), those in this subsample had higher levels

of education and personal income, visited doctors more frequently, and maintained an overall

healthier life style (e.g. non-smokers). They were, however, similar to the other respondents in

terms of other demographic (e.g., age, gender, and marital status) and health characteristics (for a

more detailed description of the study, consult Love et al. 2010).

Measures

Independent Variables

Childhood abuse history. Childhood abuse is used as a key indicator of traumatic stress

during childhood. The Childhood Trauma Questionnaire (CTQ; Bernstein and Fink 1998) is used

to evaluate the severity of physical, emotional, and sexual abuse up to the age of 16. The CTQ is

a well-validated measure that contains five-item subscales to assess each of the three different

types of abuse (emotional, physical and sexual abuse) and two different types of neglect

(emotional and physical). It also includes a three-item scale for minimization and denial to

identify respondents who are more likely to underreport negative events in childhood (e.g., "I had

the best family in the world"). Respondents answered questions about childhood abuse/neglect

and minimization/denial, which were measured on a scale ranging from 1 = "never true" to 5 =

"very often true." The analyses are based on the 15 CTQ items that assess the three types of abuse

and on the composite score from the three minimization/denial items (for details on the individual

items of childhood abuse, see Table A1-1 in the Appendix). A composite score of each domain of

childhood abuse ranges from 5 (no abuse) to 25 (extremely abuse). Latent class analysis (LCA)

are used to crate profiles of childhood abuse (for details, see "Analytic Strategy" and "Results" about LCA).

Dependent Variables

Immune-related disorders, which are known to be associated with abnormal secretion of cortisol, were selected as dependent variables. Respondents were asked two questions for each of following conditions: asthma, arthritis, and allergies, except allergies to medications. First, they were asked if they ever had each condition, and if so, whether or not a medical professional had ever diagnosed the condition. In order to reduce bias from subjective reports of health conditions, immune-related disorders are coded 1, only if they responded "yes" to both of these questions. Respondents were placed into a category of allergies (yes/no), asthma (yes/no), or arthritis (yes/no).

A Physiological Mediator

Abnormal Cortisol Secretion. To assess reduced or increased cortisol output, I use the value for the12-hour urinary cortisol concentration. Compared to salivary cortisol, 12-hour urinary cortisol provides a broader and more integrative profile of HPA activity (Nicolson 2008) and minimizes the potential confounding effects of physical activities (Seeman et al. 2004). In the GCRC, participants were instructed to collect all urine from 7 p.m. to 7 a.m. and to notify nursing staff immediately after each void. At the end of the urinary collection at 7 a.m., participants reported missed voids and urine not collected. The urinary collection for cortisol was immediately frozen and stored in a freezer set at between -60° C and -80° C and then was shipped to one of the MIDUS Bio Core laboratories. Urinary cortisol assays were performed at the Core Lab of the University of Wisconsin using Enzymatic Colorimetric Assay and Liquid Chromatography-Tandem Mass Spectrometry (Ryff et al. 2010).

To adjust for variability in urinary volume and concentration (Garde et al. 2004), I use creatinine-adjusted cortisol, which is reported as micrograms of urinary cortisol per gram of creatinine with a reference range of 0.7 to 85.0 μg cortisol/g creatinine. Based on prior studies

(Gersten 2008; Seeman et al. 2001), abnormal cortisol secretion is classified into two groups of cortisol levels: high levels of cortisol (upper 25% = 1 vs. remaining 75% = 0) and low levels of cortisol (bottom 25% = 1 vs. remaining 75% = 0). The cut-off points for low and high levels are 6.7 and 19.0 μg cortisol/g creatinine, respectively. Although the main operationalization of abnormal cortisol levels is guided by allostatic load measures (e.g., high-risk 12-hours urinary cortisol levels as the top 25% of the distribution), I also use 12-hour urinary cortisol and creatinine-adjusted 12-hour urinary cortisol to determine either the negative or positive association between childhood abuse and cortisol levels. These two cortisol measures are treated as continuous variables with natural log transformation due to skewed distributions.

Control Variables

To eliminate the possibility of potential spurious associations between childhood abuse and outcome variables through confounders, this study includes seven sets of covariates: demographics (Adam and Kumari 2009), childhood environments (Taylor et al. 2011a), socioeconomic status (SES) (Seeman and McEwen 1996), health behaviors (Nicolson 2008), mental health, social strain (Morozink et al. 2010), and medications (Adam and Kumari 2009). Demographic variables include gender (1 = female), race/ethnicity (1 = white, 0 = non-white), age of respondents at the time of MIDUS II (40-65 years old) as a linear covariate, current marital status at the time of the Bioindicator assessment (married/cohabiting = 1 vs. separated, divorced, widowed, or never married = 0) and educational attainment at MIDUS I as a categorical variable (less than high school [reference], high school, college, more than masters' degree). There is no significant curvilinear relation between age and outcome variables.

Prior studies indicate that poor childhood environments (e.g., low SES) are significantly associated with impaired immunity and immune-related disorders (Chen and Miller 2007; Miller et al. 2011a). To disentangle the effect of childhood abuse on outcome variables from other adverse childhood experiences, I include three childhood family backgrounds: the highest level of education held by a parent as a categorical variable (less than high school [reference], high

school, more than high school), whether they lived with both their biological parents until the age

of 16 (yes/no), and whether the family was on welfare or Aid to Dependent Children (ADC)

during childhood (yes/no).

Because previous studies indicate a significant association between mental health

problems (e.g., depression) and abnormal cortisol levels (Yehuda et al. 1996), I include a 10-item

perceived stress scale (PSS) questionnaire (scale reliability = .86). The composite score of the

PSS is used (mean [SD] = 22.3 [6.5]). Due to a significant association between quality of social

interaction with immune functions (Morozink et al. 2010), I also control for a measure of social

strain. Approximately one fourth of respondents have not cohabitated or married. To avoid

missing data due to marital status among respondents who did not have spouses or partners, social

strain is measured by a maximum score of strain from friends, family, or spouse/partner, ranging

from 1 (not at all) to 4 (a lot). Health behaviors, which are known to account for individual

differences in cortisol levels (Nicolson 2008), include four variables: the number of caffeinated

beverages consumed per day (0-30 cups/day), a history of smoking behavior (none/former/current

smoker), current alcohol consumption per week (0 = less than 1-2 days per week and 1 = more

than 3-4 days per week), and vigorous exercise (yes/no). Vigorous exercise is defined as regular

exercise for at least 20 minutes three times per week, such as competitive sports, running,

vigorous swimming, and high intensity aerobics. Finally, since medication use might affect

cortisol levels (Adam and Kumari 2009), I include the use of two types of medication as

inventoried by the staff of GCRC: antidepressants (yes/no) and corticosteroids (yes/no),

Analytic Strategy

Analyses are carried out in two stages. First, I use latent class analysis (LCA), to identify

subgroups of respondents with a similar history of childhood abuse. Most abused children

experience multiple types of abuse with varying degrees of severity and frequency (Cicchetti and

Toth 1993; Irving and Ferraro 2006). Given the potentially complicated nature of abuse, latent

modeling is beneficial in identifying the underlying heterogeneity of the childhood abuse

experience. LCA has been well-employed to identify a set of heterogeneous subgroups based on the patterns of responses to given observed categorical variables (Collins and Lanza 2010). I use 15 items from the CTQ for the LCA. Each type of abuse includes five items (see Appendix Table A1-1 for details).

To achieve a manageable number of cells and to avoid unacceptable sparse distributions within cells in the latent analysis data matrix, I recode the five initial response categories of the CTQ items into a dichotomized response for each item (0 = "never" and "rarely true" and 1= "sometimes," "often," and "very often true") (see note 2). In the LCA, I add a composite score of the three items of minimization/denial (e.g., "I had the perfect childhood") as a control variable to adjust for the response tendency among some respondents who may have exaggerated positive aspects of or denied negative experiences during their childhood (Bernstein and Fink 1998).

To select the best model fit (optimal number of latent classes) in subsequent comparisons between k and $k+1$ class solutions, I use the Akaike Information Criterion (AIC), the Bayesian Information Criterion (BIC), entropy, the Lo-Mendell-Rubin Likelihood Ratio Test (LRT), and interpretability(Collins and Lanza 2010; Lo et al. 2001). It is important to understand descriptive information of abuse categories and how different profiles of abuse affect abnormal cortisol secretion and immune-related disorders for subsequent analyses.

Regarding the labeling of LCA classes, I use the cutoff scores recommend in the CTQ manual (Bernstein and Fink 1998) and the pattern of item response probabilities produced by LCA (see note 3 for cutoff scores and see Tables 1-1 for the scores of each domain across LCA classes). After determining the latent class of childhood abuse, I use F-tests and χ^2-tests to compare individual characteristics across latent classes of childhood abuse. I expect that individuals who experienced high levels and multiple types of childhood abuse have poorer outcomes.

In the second stage, based on a well-established mediation analysis approach (Baron and Kenny 1986), I conduct a series of analyses to assess associations between the diverse profiles of

childhood abuse and immune-related disorders. First, multivariate binary logistic regression analyses are used to determine the associations between childhood abuse and each immune-related disorder after adjusting for all covariates. Latent classes are entered into the models as a series of dummy variables, with the reference group comprising respondents who did not experience childhood abuse. I also test whether there are significant differences in risk of developing immune-related disorders among the groups that include victims of childhood abuse. Second, I assess the associations between the childhood abuse profiles and abnormal cortisol levels after adjusting for the covariates. Third, I examine the association between the cortisol levels and immune-related disorders. Finally, I assess the mediating influence of cortisol on the effect of childhood abuse on the immune-related disorders. The significance tests of indirect and direct effects are confirmed using 95% bias-corrected bootstrap confidence intervals based on 1000 bootstrap replications (for details, see note 4).

The percentage of missing data is approximately 9% when listwise deletion is applied. I impute data under the missing-at-random assumption in order to alleviate potential loss of statistical power in subsequent analyses (Allison 2001). All variables except the dependent variables and the mediator are included in the imputation procedure. The analyses are carried out using Mplus 6.0 (Muthén and Muthén 2008; Muthén and Muthén 2010) and STATA 11.0 (STATA Corp, 2010). Since respondents from the same family (e.g., 13% twins or siblings in the biomarker study) are likely to be similar in many ways (e.g., health behaviors, history of illness, genes), compared to the other respondents from different families, I apply robust standard error estimation to correct intra-class correlation.

Results

Latent Classes of Childhood Abuse and Their Characteristics

The LCA results show that the five-class solution fits the data the best (see Table A1-2 in Appendix). The patterns of results for the five classes are represented graphically in Figure 1-1. In the figure, the y-axis indicates the item response probabilities (i.e., the proportion of

responding "sometimes," "often," or "very often true" vs. "never" or "rarely true" to each of the 15 CTQ items), and the x-axis indicates the individual CTQ items with abbreviations (see Table A1-1 in Appendix, for full descriptions of each item). In the legend, the latent class probabilities (%) and the size of each class (n) are reported. Based on the pattern of item response probabilities for each class in Figure 1-1, the five classes are labeled as: Class1= no abuse (65.7%, n = 590); Class2 = low emotional abuse (EA)/no physical abuse (PA)/low sexual abuse (SA) (16.8%, n = 151); Class3 = no EA/PA and high SA (6.2%, n = 56); Class4 = high EA/PA/low SA (5.0%, n = 45); and Class5 = high EA/PA/SA (6.2.%, n = 56).

[Figure 1-1 about here]

Table 1-1 contrasts the individual characteristics of the latent classes of childhood abuse. Overall, victims of childhood abuse are more likely to come from disadvantaged backgrounds and have more health problems than those who did not experience such abuse. With respect to gender, the two groups of sexually abused respondents (Class3 and Class5) consist of a higher percentage of women than the other groups consisting of non-sexually abused respondents. The respondents in the low EA/no PA/low SA and the high EA/PA/SA groups are less likely to be currently married or cohabiting than those in the other groups. Victims of childhood abuse grew up with less-educated parents than the non-abused. The respondents in the high EA/PA/SA group were less likely to have lived with their biological parent(s) up until the age of 16 years and their families were more likely to have received welfare or ADC.

The respondents who experienced no EA/PA with high SA, compared to those in the other groups, are more likely to take corticosteroids. The respondents who experienced sexual abuse (Class3, Class4 and Class5), compared to the other respondents who did not experience it (Class1 and Class2), are more likely to take antidepressant medications. Victims of childhood abuse, compared to non-victims, have poorer health behaviors except alcoholic drinking and have higher levels of both perceived stress and social strain. Victims of childhood abuse are more likely than non-victims to report having allergies, asthma, and arthritis and to be in the bottom

25% of cortisol, rather than upper 25% of cortisol, yet the difference was not statistically significant. Thus, in the next step, I test whether the association between childhood abuse and the abnormal cortisol secretion is significant after controlling for the covariates.

[Table 1-1 about here]

Associations between Childhood Abuse and Abnormal Cortisol Secretion

Table 1-2 shows how childhood abuse is associated with cortisol levels. To evaluate the association between childhood abuse and bidirectional cortisol secretion, I analyze the extremes (bottom 25% and upper 25% of cortisol) of creatinine-adjusted 12-hour urinary cortisol, as well as perform linear regressions on continuous measures of both creatinine-adjusted and non-adjusted 12-hour urinary cortisol. All covariates are included in the models. The overall results consistently show that respondents who experienced childhood abuse, compared to those who did not, tend to have lower levels of cortisol in adulthood. Specifically, compared to non-victims of childhood abuse (Class1), individuals who experienced high EA/PA/SA (Class5) are nearly two times as likely to have cortisol levels in the bottom 25%. Similarly, compared to non-victims, individuals who experienced all types of severe abuse have a lower level of creatinine-adjusted 12-hour urinary cortisol (estimated coefficient = .28). The pattern of associations is similar in the other abused groups, although it is not statistically significant. In contrast, respondents who experienced childhood abuse, compared to those who did not, are less likely to have high levels of cortisol (upper 25%), yet this association is not statistically significant.

To investigate the association between hypocortisolism and severe childhood abuse, I also conduct supplementary analyses to test whether individuals who experienced high levels of all types of abuse are more likely to have even more extreme levels of cortisol (bottom 15% and bottom 10%). I confirm that compared to non-victims, victims of severe abuse are 2.69 times more likely to be in the bottom 15% of the cortisol distribution ($p < .01$) and 2.19 times more likely to be in the bottom 10% of the cortisol distribution (p < .07), even after controlling for all covariates. There are no significant associations at the upper 10% or 15%.

To summarize, compared to non-abused respondents, those who experienced high levels of EA/SA/PA as children are more likely to exhibit low cortisol levels in adulthood. There is no evidence that victims of childhood abuse, compared to non-victims, have higher cortisol levels at midlife. These results from population-based data provide strong evidence in support of the association, as established in previous literature, between childhood abuse and hypo-cortisol levels.

[Table 1-2 about here]

Associations between Cortisol Levels and Immune-Related Disorders

Table 1-3 shows how cortisol levels are associated with immune-related disorders after accounting for all covariates. Both hypo- and hyper-cortisol levels are used as independent variables. Overall, there are significant negative associations between cortisol levels and risk of immune-related disorders; having cortisol levels in the bottom 25%, compared to the upper 75%, puts individuals at increased risk for developing allergies, asthma, and arthritis, while having cortisol levels in the upper 25%, compared to the bottom 75%, puts individuals at decreased risk of developing those immune-related disorders. Both creatinine-adjusted 12-hour urinary cortisol and 12-hour urinary cortisol are negatively associated with risk of immune-related disorders. The results provide evidence that low cortisol levels are associated with immune-related disorders for individuals in midlife.

[Table 1-3 about here]

A Biological Pathway Linking Childhood Abuse and Immune-Related Disorders through Abnormal Cortisol Secretion

Table 1-4 shows the extent to which low cortisol levels (bottom 25%) explains the association between childhood abuse and immune-related disorders. The difference between model 1 and model 2 in Table 1-4 is that I add cortisol level (bottom 25% compared to upper 75%) as a biological mediator. Overall the results show that all abused groups, compared to the no-abuse group, have a higher prevalence of allergies, asthma, and/or arthritis. Furthermore,

supplementary analyses (data available up on request) show that the individuals who experienced

high SA (Class3 and Class5) have a higher prevalence of arthritis, compared to those who

experienced low EA/no PA/low SA (Class 2). Specifically, individuals who experienced all types

of high abuse (Class5) are more likely than non-victims of childhood abuse (Class1) to develop

all three immune disorders, including allergies ($OR = 2.54$, $p < .01$), asthma ($OR = 2.44$, $p < .05$),

and arthritis ($OR = 2.89$, $p < .01$). After accounting for cortisol level, the effects are slightly

attenuated for allergies ($OR = 2.37$, $p < .01$), asthma ($OR = 2.26$, $p = .07$), and arthritis ($OR =

2.75$, $p < .01$). The indirect effect is significant for allergies ($p < .05$) and arthritis ($p < .05$) but

not for asthma. The proportion of the total effect that is mediated is not large (11% for allergies

and 7% for arthritis).

Similarly, individuals, who experienced no PA/EA with high SA (Class3), compared to

non-victims of childhood abuse (Class1), are more likely to have all three immune-related

disorders. Compared to non-victims, individuals who experienced high EA/PA with low SA

(Class4) are more likely to have allergies. Individuals with a history of low EA/no PA/low SA

(Class2) are more likely to have allergies and asthma than non-victims of childhood abuse. Yet,

having cortisol levels in the bottom 25% of the sample does not significantly explain why

individuals in these abuse groups (Classes 2 through 4) have developed allergies and/or asthma.

After accounting for history of childhood abuse, individuals who have very low levels of cortisol

(bottom 25%) are more likely to have allergies ($OR = 1.60$, $p < .01$), asthma ($OR = 1.64$, $p < .05$)

and arthritis ($OR = 1.58$, $p < .05$), compared to those who have higher levels of cortisol (the

remaining 75%).

To summarize, the results show that hypocortisolism helps to explain the associations

between a history of high PA/EA/SA and two immune-related disorders (allergies and asthma).

However, the extent of this effect is small, just 7% for arthritis and 11% for allergies. After

adding this biological mechanism, however, childhood abuse still remains a significant predictor

of these disorders. Cortisol also has an independent effect on immune-related disorders, after controlling for childhood abuse.

[Table 1-4 about here]

Discussion

This study, which examines childhood abuse as a risk factor for immune-related disorders during adulthood as mediated by abnormal cortisol levels, yields four major findings. First, I find that there exist five classes of childhood abuse, each of which reflects a distinct combination of various subtypes of abuse and the severity of each type of abuse. Second, I find that respondents who experienced childhood abuse, compared to those who did not, are more likely to have immune-related disorders at midlife. The greater the severity of abuse, the higher the risk of developing a disorder. Sexual abuse, in particular, plays an important role. Respondents who reported experiencing high levels of sexual abuse, regardless of the severity of other types of abuse, are more likely to have allergies, asthma, and arthritis, compared to those who did not report experiencing sexual abuse.

These findings suggest that both the severity and type of childhood abuse should be considered in determining the effect of abuse on risk of developing immune related-disorders. My findings are consistent with prior research which links childhood maltreatment to increased risk of developing asthma (Lanier et al. 2010) and physical abuse to increased risk of developing arthritis (Fuller-Thomson et al. 2009). While prior studies focused on the effect of a certain type of childhood abuse or the overall experience of childhood maltreatment on particular immune-related disorders, I use a population-based sample to examine the extent to which different profiles of childhood abuse are related to three different types of immune-related disorders. I also use a range of controls, including family background and other childhood adversities, which helps reduce spurious associations between profiles of childhood abuse and risk of developing immune-related disorders. Regarding the association between sexual abuse and immune-related disorders, the literature documents that women have more severe immune responses than men and that

women are more likely to develop immune-related disorders in adulthood, such as rheumatoid arthritis (Morell 1995) and asthma (Postma 2007). The high prevalence of sexual abuse among women and their heightened vulnerability to immune-related diseases might explain why this study shows that respondents who experienced high sexual abuse are more likely to have immune-related disorders.

Third, in terms of the association between childhood abuse and cortisol levels, I find that individuals who experienced abuse during childhood are more likely to have low levels of cortisol rather than high levels of cortisol in midlife. Furthermore, individuals who suffered high levels of multiple types of abuse are more likely to have low cortisol levels. Compared to individuals who experienced low or medium levels of childhood abuse, those who experienced high levels of childhood abuse have lower cortisol levels. These findings are consistent with the findings of other studies of childhood abuse and hypocortisolism, including those that have linked sexual abuse to abnormality of diurnal cortisol rhythms (Trickett et al. 2010); the experience of sexual abuse to decreased levels of adrenocortical reactivity (Kaufman et al. 1997); and low levels of parental affection during childhood to flat diurnal cortisol rhythms (Taylor et al. 2011a). I extend previous studies by investigating the association between diverse profiles of childhood abuse and bidirectional cortisol abnormality.

Fourth and last, I find some evidence that low levels of cortisol partially mediate the association between childhood abuse and immune-related disorders. Individuals who experienced high levels of childhood abuse, compared to those who did not, are more likely to have immune-related disorders. Part of this association is explained by low levels of cortisol (i.e., being in the bottom 25%). Yet, the indirect effect explained by cortisol is only significant for the outcomes of arthritis and allergies. This finding somewhat supports emerging theories related to stress, hypocortisolism, and immune-related disorders (Fries et al. 2005; Heim et al. 2000a; Raison and Miller 2003), suggesting that a lack of cortisol leads to an unregulated immune system, pathological inflammatory activities, and, ultimately, immune-related disorders. While previous

studies find connections between childhood abuse, cortisol abnormalities, and immune-related disorders, my study contributes to the literature by linking diverse profiles of childhood abuse, both high and low cortisol abnormalities, and three immune-related disorders in a population-based study.

Several plausible explanations might account for why victims of high childhood abuse are more likely than non-victims to develop immune-related disorders through hypocortisolism. The experience of extreme abuse as children might directly affect parts of the brain related to the secretion of stress hormones in the HPA axis (de Bellis et al. 1994; Lupien et al. 2009). Individuals who are exposed to adverse circumstances in early life have a greater chance of being exposed to secondary adversities in later life (Ferraro and Shippee 2009). Individuals who experienced childhood trauma might further develop maladaptive coping skills, such as avoidance, anxiety-related behaviors, and self-destructive behaviors, rather than more positive problem-solving behaviors (Runtz and Schallow 1997). They might engage in unhealthy behaviors (Bentley and Widom 2009) and receive insufficient social support (Gotlib and Wheaton 1997). In addition, they often have low SES (Currie and Widom 2010), which in turn increases their risk of being exposed to poor physical environments, such as poor housing, toxins, and allergens. Therefore, either by direct or indirect pathways, the experience of severe childhood abuse might increase individuals' risk of developing hypocortisolism and immune-related disorders in adulthood.

Limitations and Future Directions

This study has five limitations that have implications for interpreting its findings. First, given the cross-sectional nature of the biomarker data, it is not possible to definitively ascertain the causal ordering of cortisol levels and immune-related disorders. I could not test the development of immune-related disorders through the onset of abnormal cortisol secretion over the life course. There is a possibility of reverse causality between abnormal cortisol secretion and immune-related disorders. For example, individuals who have health conditions related to

extremely low cortisol levels (e.g., Addison's disease) or immune-related diseases (e.g., asthma) are more likely to take corticosteroid medications. Research indicates that long-term use of corticosteroids might alter the HPA axis, which in turn results in reduced cortisol secretion (Dluhy 1998).

To evaluate the plausibility of reverse causation (whereby immune-related disorders affect cortisol levels), I create a subsample which only includes respondents who have a history of allergies, asthma, and/or arthritis (n = 537) and conduct two separate analyses: 1) I evaluate the extent to which childhood abuse is associated with cortisol levels, and 2) I test the extent to which childhood abuse is associated with being in the bottom quartile of cortisol levels. I find that among individuals with a history of any of the three immune-related disorders, victims of severe childhood abuse, compared to non-victims, have significantly lower levels of cortisol (estimated coefficients = .33). Furthermore, individuals who experienced sexual abuse (Class3 and Class5) are more likely to be in the bottom quartile of cortisol levels than non-victims of childhood abuse. These results provide some evidence that lower levels of cortisol partially explain why victims of childhood abuse are at greater risk of developing immune-related disorders. To more rigorously test for causal association, future studies should explore these associations using data collected at various points in time throughout childhood and adulthood.

Second, there might be a recall bias in reporting childhood abuse since questions about abuse were asked in midlife. As previous studies point out, there exists the possibility that individuals with mood disorders might exaggerate or misrepresent their adversities during childhood (White et al. 2007; Widom and Morris 1997). Nonetheless, recent studies report that memories of specific childhood experiences are highly stable (Yancura and Aldwin 2009), and delayed recollection of traumatic memories, such as childhood abuse, tends to be fairly accurate (Hardt and Rutter 2004). In supplementary analyses, I also find strong correlation and consistency between reports of physical abuse at MIDUS I and MIDUS II (correlation = .76 and Cohen's kappa = 84.5%). Given the use of slightly different measures (Conflict Tactics Inventory in

MIDUS I and CTQ in MIDUS II) that were collected 10 years apart, the measures of self-reported childhood abuse in this study appear quite reliable. In addition, research on individuals' appraisals of stressful events and the various coping strategies used to deal with them has pointed out the importance of considering an individual's subjective perception of stressors (Lazarus and Folkman 1984). That is, the way that victims of childhood abuse assess the adversity of early life events might explain whether they adopt negative or positive coping strategies and their concomitant health consequences.

Third, this study does not include respondents who experienced only childhood neglect due to the relatively small size of the sample when I applied latent class analysis and owing to strong correlations between experience of childhood abuse and neglect in the sample. Although most prior studies have identified childhood abuse as a key predictor of traumatic stress, recent studies have reported that childhood neglect may also substantively influence cortisol levels (van der Vegt et al. 2009). Therefore, future research should consider including a broader definition of childhood maltreatment in a larger sample.

Fourth, although overnight 12-hour urinary cortisol collection mitigates potential noise, such as vigorous physical activity, which affects the fluctuation of cortisol, this study does not control for other factors, such as body mass index (BMI) or sleep quality, which might partially account for individual differences in cortisol levels (Adam and Kumari 2009; Nicolson 2008). There might be other drawbacks in the measure of cortisol used in this study since urinary cortisol secretion might not fully reflect HPA activity and also depends on cortisol metabolism (Nicolson 2008). Therefore, future research should consider replicating my study using different measures of cortisol.

Finally, I considered a limited set of predictor variables. Unobserved and unmeasured factors in this study might potentially explain the rest of the variation in the associations between childhood abuse and immune-related disorders. Genetic vulnerability is known to affect immune-related disorders (Ober and Hoffjan 2006). Parents' medical history, such as depression, is

associated with the levels of cortisol of their children (Halligan et al. 2004) and with their children's risk of having asthma (Turney 2011). Similarly, risk of immune-related disorders might be affected by environmental factors, such as exposure to chemicals, crowded housing environments, tobacco smoking, and other adverse neighborhood characteristics (Chen and Miller 2007). Accordingly, it is important that future research include these factors as potential confounders.

Despite these limitations, there is much to be learned from this study. My findings contribute to the limited number of studies related to the effects of early life stressors on the development of diseases through biological pathways. Using latent class analysis, I identify meaningful subgroups of individuals with similar histories of childhood abuse. Adopting new theories regarding bidirectional cortisol levels, I provide useful guidance about how to operationalize abnormal levels of cortisol distribution. Despite my contributions, there is a need for better identification of the social, behavioral, psychological, and biological mechanisms that account for the health consequences of childhood abuse over the life course. Understanding these complex mechanisms can shed light on how to improve social services and public health interventions for those who have experienced such adversities during childhood.

Notes

1. According to Heim et al. (2000), hypocortisolism is defined as insufficiency of cortisol, which might be attributable to three biological conditions: 1) reduced adrenocortical secretion; 2) reduced adrenocortical reactivity; or 3) increased sensitivity of the HPA axis to negative feedback inhibition, which suppresses cortisol secretion. Hypocortisolism can be observed by different measures of the HPA axis hormones: 1) decreased 24-hour or 12-hour urinary cortisol levels (Yehuda et al. 1995b); 2) low-morning cortisol (Trickett et al. 2010; van der Vegt et al. 2009); 3) flat diurnal cortisol rhythms (Taylor et al. 2011a); 4) an increased number of glucocorticoid receptors for negative feedback activity (Yehuda et al. 1995a); and 5) diminished ACTH secretion (Heim et al. 2001).

2. I treat the frequency of experiencing each CTQ item equally (1 = sometimes, often, very often true vs. 0 = never and rarely true). Across the 15 CTQ items, I acknowledge that some (e.g., "I felt that someone in my family hated me") reflect less severe forms of abuse than others (e.g., "Someone tried to make me do sexual things or watch sexual things"). As such, the effect of some forms of abuse (e.g., emotional) might be less harmful than the effect of other forms of abuse (e.g., sexual) in terms of influencing risk of developing chronic diseases.

3. The CTQ manual provides the following cutoff scores for each type of abuse: 1) emotional abuse: no (5-8), low (9-12), medium (13-15), and high (16-25); 2) physical abuse: no (5-7), low (8-9), medium (10-12), and high (13-25); and 3) sexual abuse: no (5), low (6-7), medium (8-12), and high (13-25).

4. For the bootstrap procedure, see UCLA: Academic Technology Services, Statistical Consulting Group, How can I perform mediation with binary variables? Available at http://www.ats.ucla.edu/stat/stata/faq/binary_mediation.htm. Accessed November 11, 2011.

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Table 1-1 Bivariate Analysis: Characteristics of Latent Classes of Childhood Abuse (n = 898)

Latent classes of childhood abuse	Class1 (65.7%, n = 590) No abuse		Class2 (16.8%, n = 151) Low EA No PA Low SA		Class3 (6.2%, n = 56) No EA/PA High SA		Class4 (5.0%, n = 45) High EA/PA Low SA		Class5 (6.2%, n = 56) High EA/PA/SA		χ^2 (df) or F- test
	Mean/%	SD	Mean/%	SD	Mean/%	SD	Mean/%	SD	Mean/%	SD	
Immune-related disorders											
Allergies	38		46		54		49		54		13.0 (4)*
Asthma	10		17		22		16		20		13.9 (4)**
Arthritis	28		26		49		41		58		33.4 (4)***
Abnormal cortisol secretion											
Bottom 25% vs. Remaining 75%	23		28		30		31		38		8.16 (4)
Upper 25% vs. Remaining 75%	29		27		21		18		18		5.9 (4)
Controls											
White	79		75		77		82		57		15.4 (4)**
Female	51		57		86		44		82		43.3 (4)***
Age (40-65)	52.6	7.5	51.9	6.8	52.1	7.0	51.3	5.4	50.3	6.4	1.77 (4)
Married/Cohabitating	69		58		66		67		50		13.3 (4)*
SES											
≤ High school	27		25		32		38		25		16.0 (12)
< College	28		28		34		27		45		
College	22		20		11		20		14		
≥ Master degree	23		27		23		16		16		
Childhood environments											
Parental education											
< High school	20		19		36		24		50		38.6 (8)*
High school	35		34		38		38		30		
> High school	45		46		27		38		20		
Living with parents by age 16	80		74		77		73		61		17.8 (4)*
Family on welfare	5		9		11		11		39		77.3 (4)***

Perceived stress	21.0	5.7	24.0	7.46	24.3	6.6	25.6	7.6	26.7	7.1	20.2 (4)***
Social strain (1 = not at all ~ 4 = a lot)	2.00	0.5	2.2	0.50	2.0	0.4	2.1	0.6	2.2	0.6	8.7(4)***
Health behaviors											
Never smoked	54		50		57		38		45		19.9 (8)*
Former smoker	31		32		30		27		27		
Current smoker	15		17		13		35		29		
Alcoholic drinking ($\geq$ 3-4 days per week)	23		24		13		13		7		13.1 (4)*
Drinking caffeinated beverages (0~30/day)	3.7	3.4	3.4	3.2	3.9	3.5	5.3	5.4	2.9	2.1	3.7(4)**
Medications											
Steroids	11		11		21		4		11		7.6 (4)
Antidepressants	13		16		23		20		27		11.9 (4)*
Childhood Abuse (5-25)[a]											
Emotional abuse	6.0	1.3	11.4	3.1	8.1	2.3	16.3	5.9	17.6	4.0	589.9 (4)***
Physical abuse	5.9	1.2	7.1	1.8	7.2	1.9	14.9	3.8	14.0	4.8	412.2 (4)***
Sexual abuse	5.2	1.2	5.5	1.2	14.6	4.4	5.8	1.5	18.2	4.9	875.2 (4)***

Note.[a]5 = no abuse ~ 25 = extreme abuse.

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

Abbreviations. EA = emotional abuse; PA = physical abuse; SA = sexual abuse.

Table 1-2 Multivariate Logistic and OLS Regression Models for the Association between Latent Classes of Childhood Abuse and Cortisol Measurements

	Binary Logistic Regression Models		OLS Regression	
	Bottom 25% of cortisol	Upper 25% of cortisol	Creatinine-adjusted 12-hour urinary cortisol	12-hour urinary cortisol
	OR (95% CI)	OR (95% CI)	Coefficient (SE)	Coefficient (SE)
No abuse				
Low EA/No PA/Low SA	1.26 (.82-1.94)	.92 (.61-1.39)	-.07 (.06)	-.05 (.08)
No EA/PA/High SA	1.78 (.93-3.39)	.56 (.28-1.11)	-.07 (.10)	-.11 (.13)
High EA/PA/Low SA	1.63 (.80-3.35)	.45 (.19-1.08)	-.11 (.11)	-.21 (.14)
High EA/PA/SA	2.14 (1.10-4.18)*	.48 (.21-1.10)	-.28 (.11)*	-.22 (.14)

Note. All control variables (demographics, childhood environments, SES attainment, health behaviors, mental health, social support, and medications) are adjusted for the models.

Abbreviations. OR = Odds Ratio; CI = Confidence Interval; SE = standard error; EA = emotional abuse; PA = physical abuse; SA=sexual abuse.

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

Table 1-3 Multivariate Binary Logistic Models for the Association between Cortisol Levels and Immune-Related Disorders

	Allergies (n = 895)	Asthma (n = 891)	Arthritis (n = 881)
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Bottom 25% vs. Remaining 75% of cortisol (Reference)	1.68 (1.21-2.33)**	1.75 (1.11-2.75)*	1.65 (1.18-2.32)**
Upper 25 % vs. Remaining 75% of cortisol (Reference)	.70 (.51-.97)*	.52 (.30-.92)*	.68 (.47-.96)*
Creatinine-adjusted 12-hour urinary cortisol	.68 (.55-.84)***	.60 (.44-.83)**	.68 (.55-.85)**
12-hour urinary cortisol	.84 (.71-.98)*	.72 (.59-.88)**	.82 (.70-.97)*

Note. All control variables (demographics, childhood environments, SES attainment, health behaviors, mental health, social support, and medications) are adjusted for in the models.
Abbreviations. OR = Odds ratio; CI = Confidence Interval.
*p < .05; ** p <.01; *** p <.001.

Table 1-4 Multivariate Logistic Regression Models for the Association between Latent Classes of Childhood Abuse and Immune-Related Disorders

	Allergies (n = 895)		Asthma (n = 891)		Arthritis (n = 881)	
	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 1 OR (95% CI)	Model 2 OR (95% CI)
Childhood abuse						
No abuse	1.00	1.00	1.00	1.00	1.00	1.00
Low EA/No PA/Low SA	1.55 (1.05-2.30)*	1.53 (1.02-2.28)*	2.11 (1.19-3.75)*	2.06 (1.16-3.66)*	.82 (.53-1.28)	.81 (.51-1.26)
No EA/PA/High SA	2.06 (1.13-3.77)*	1.99 (1.11-3.57)*	2.30 (1.05-5.05)*	2.19 (1.00-4.78)	2.02 (1.11-3.66)*	1.92 (1.06-3.49)*
High EA/PA/Low SA	2.25 (1.17-4.32)*	2.18 (1.13-4.20)*	2.37 (.92-6.17)	2.33 (.90-6.03)	1.83 (.90-3.71)	1.78 (.88-3.57)
High EA/PA/SA	2.54 (1.36-4.43)**	2.37 (1.27-4.43)**	2.44 (1.01-5.96)*	2.26 (.91-5.58)	2.89 (1.48-5.62)**	2.75 (1.40-5.38)**
Bottom 25% vs. Remaining 75% of cortisol (reference)		1.60 (1.15-2.21)**		1.64 (1.03-2.61)*		1.58 (1.12-2.22)*
χ^2; df	63.41; 23	73.85; 24	70.74; 23	73.37; 24	86.86; 23	86.86; 24
Pseudo R^2	.058	.065	.112	.118	.102	.107

Note. All control variables (demographics, childhood environments, SES attainment, health behaviors, mental health, social support, and medications) are adjusted for in the models.

Abbreviations. OR = Odds Ratio; CI = Confidence Interval; EA = emotional abuse; PA = physical abuse; SA = sexual abuse.

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

Figure 1-1 Profiles of Childhood Trauma Questionnaire (15 items) for the 5-Class Solution

Probability of responding "sometimes, often, very often true" to the CTQ items

Emotional Abuse   Phyiscal Abuse   Sexual Abuse

Class1, 65.7%, n=590   Class2, 16.8%, n=151   Class3, 6.2%, n=56   Class4, 5.0%, n=45   Class5, 6.2%, n=56
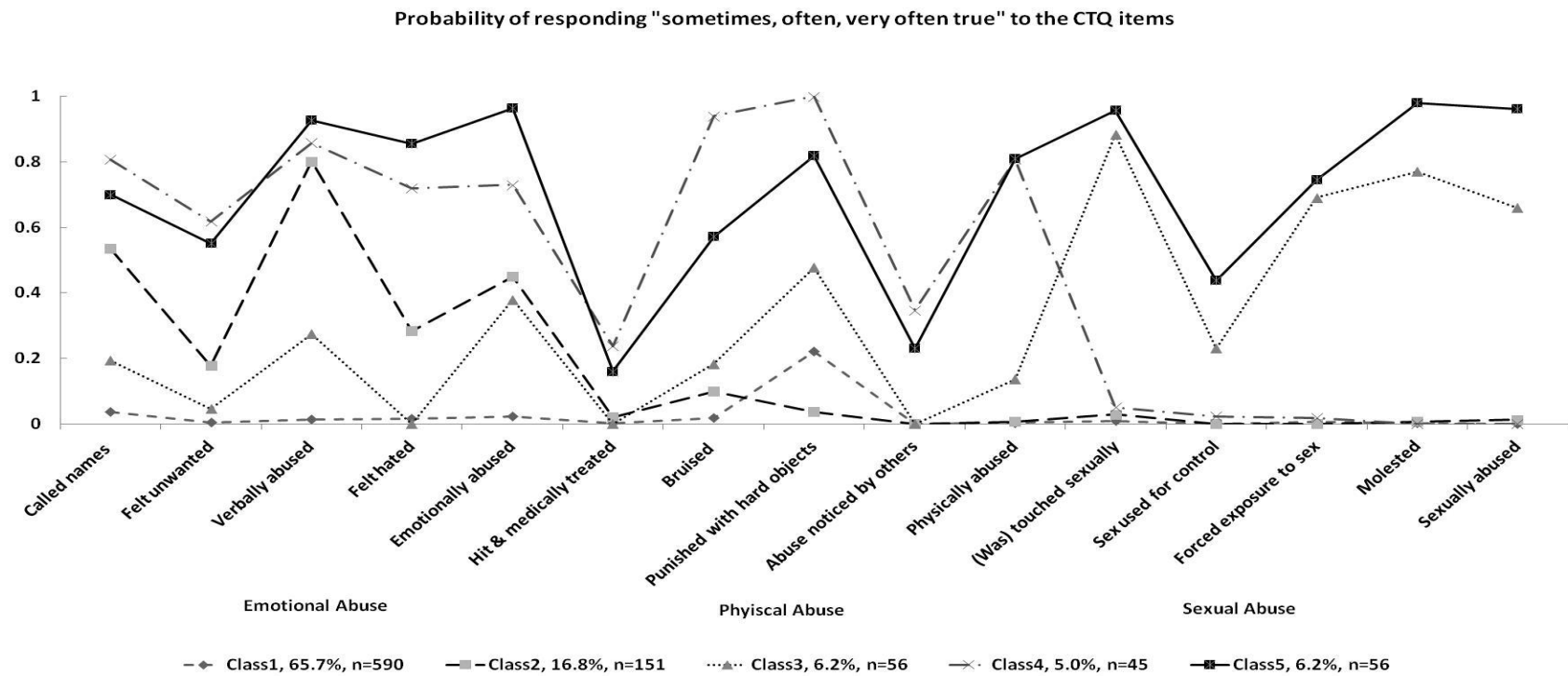
Note. Class1 = no abuse; Class2 = low EA/no PA/low SA; Class3 = no EA/PA/high SA; Class4 = high EA/PA/low SA; and Class5 = high EA/PA/SA.
Abbreviations. EA = emotional abuse; PA = physical abuse; SA = sexual abuse.

Appendix

Table A1-1 Childhood Trauma Questionnaire Items (CTQ) Used in the Analyses

Type	Items	Abbreviation
Emotional Abuse (α = .83)	People in my family called me things like "stupid," "lazy," or "ugly."	Called names
	I thought that my parents wished I had never been born.	Felt unwanted
	People in my family said hurtful or insulting things to me.	Verbally abused
	I felt that someone in my family hated me.	Felt hated
	I believe that I was emotionally abused.	Emotionally abused
Physical Abuse (α = .69)	I got hit so hard by someone in my family that I had to see a doctor or go to the hospital.	Hit & medically treated
	People in my family hit me so hard that it left me with bruises or marks.	Bruised
	I was punished with a belt, a board, a cord, or some other hard object.	Punished with hard objects
	I believe that I was physically abused.	Physically abused
	I got hit or beaten so badly that it was noticed by someone like a teacher, neighbor, or doctor.	Abuse noticed by others
Sexual Abuse (α = .92)	Someone tried to touch me in a sexual way, or tried to make me touch them.	(Was) touched sexually
	Someone threatened to hurt me or tell lies about me unless I did something sexual with them.	Sex used for control
	Someone tried to make me do sexual things or watch sexual things.	Forced exposure to sex
	Someone molested me.	Molested
	I believe that I was sexually abused.	Sexually abused
Minimization/Denial (α = .81)	There was nothing I wanted to change about my family.	
	I had the perfect childhood.	
	I had the best family in the world.	

Table A1-2 Fit Indices for Latent Class Model

	AIC[a]	BIC[a]	Entropy[d]	LRT[c]	Size of classes: n, %	
Class 3	6906.71	7141.92	.94	642.48*	1: n = 168, 18.7% 3: n = 621, 69.1%	2: n = 109, 12.1%
Class 4	6657.65	6974.46	.95	280.63*	1: n = 56, 6.2% 3: n = 166, 18.5%	2: n = 58, 6.5% 4: n = 618, 68.8%
Class 5	6474.49	6872.91	.93	215.30*	1: n = 65, 6.2% 3: n = 45, 5.0 % 5: n = 56, 6.2%	2: n = 152, 16.9% 4: n = 589, 65.6%
Class 6	6408.58	6888.59	.93	99.06	1: n = 133, 14.8% 3: n = 58, 6.4% 5: n = 41, 4.6%	2: n = 45, 5.0% 4: n = 582, 64.8% 6: n = 39, 4.3%

*Note: *p <. 05*
[a]Lower AIC and BIC values indicate better model fit.
[b]Entropy should be greater than .07; values close to 1 indicate better model fit.
[c]Less than .05 *p*-value of Lo-Mendell-Rubin LRT test indicates that k-1 classes are sufficient and k classes are not needed.
In addition to these indices, interpretability and theoretical expectation are important factors to determine the number of classes.

Chapter 3-Childhood Abuse and Metabolic Syndrome in Men and Women in Midlife: Poor Sleep Quality and Stress-Induced Eating as Potential Mechanisms

Abstract

Research indicates that traumatic stressors, such as childhood abuse, are associated with elevated levels of metabolic risk factors (e.g., abdominal obesity, glucose intolerance, high blood pressure, and high bad and low good cholesterol levels) in adulthood, which contribute to the development of metabolic syndrome (MetS). Few studies, however, have investigated directly the effects of childhood abuse on MetS. In addition, gender differences in profiles of childhood abuse and underlying mechanisms, which may link childhood abuse and MetS, are not well-understood. This study examines the associations between childhood abuse and MetS in men and women in midlife; specifically how these associations are mediated by poor sleep quality and stress-induced eating. Data come from a biomarker study of the National Survey of Midlife Development in the United States (n = 1,255). I adopt the world-wide definition of MetS used by the International Diabetes Federation. Due to gender differences in the prevalence of MetS throughout the life course, I use two different measures of MetS: MetS diagnosis and MetS components. I use latent class analysis to identify distinct classes of childhood abuse that reflect a combination of the type of abuse and the frequency of each type. I find that the number of classes based on these combinations differs by gender: five for women and four for men. The results indicate that not all individuals who experience childhood abuse are at greater risk of developing MetS. For women, high sexual abuse, along with other types of high abuse, increases risk of developing MetS. For men, medium emotional and high physical abuse, but low sexual abuse, increases the number of MetS components. Although abused individuals of both sexes are more likely to report poor sleep

quality and stress-induced eating than those who were not abused, these two factors do not significantly mediate the association between childhood abuse and MetS for either men or women. My findings suggest that gender differences in profiles of childhood abuse are important for explaining the associations between childhood abuse and MetS.

Keywords

Introduction

Metabolic syndrome (MetS) is characterized by a combination of abdominal obesity plus two of the following metabolic disturbances: glucose intolerance, high blood pressure, low good and high bad blood cholesterol levels (Alberti et al. 2006). MetS is a major risk factor for cardiovascular disease, coronary heart disease, and stroke, which are among the leading causes of adult mortality in the U.S. (Ford 2005). As the prevalence of obesity has significantly increased among the U.S. population over the past three decades, MetS is becoming more common for adults (Baskin et al. 2005), dramatically raising health care costs. For example, individuals who have MetS or diabetes incur twice the annual health care costs of those who do not have either of these conditions (Boudreau et al. 2009). Given the cost of medical expenditures and MetS-related mortality rates, MetS burdens individuals, health care systems, and society as a whole.

Several factors are significantly associated with the development of MetS. Prior studies that employ life course frameworks (Elder Jr 1995; Ferraro and Shippee 2009) find that early life adversities, such as childhood abuse, are associated with an elevated risk of single or multiple components of MetS in young adulthood (Bentley and Widom 2009; Danese et al. 2009; Noll et al. 2007) and in midlife (Greenfield and Marks 2009; Thomas et al. 2008). Given that chronic stressors detrimentally influence health, with effects that may stretch throughout the life course, the more severe the childhood abuse experienced, the greater the risk that an individual will develop MetS. Yet, prior studies have not examined how distinct profiles of childhood abuse affect the risk of developing MetS.

Gender is one factor related to increased risk of MetS; due to genetic and hormonal advantages, women are less likely than men to develop MetS prior to menopause (Carr 2003). Gender also critical in determining the nature of childhood abuse and the strategy an individual uses to cope with stress, both of which influence risk of developing MetS. For example, women are more likely than men to experience sexual abuse as children (Sedlak et al. 2010). Studies have shown that women are more likely to use binge eating to cope with stress (Tanofsky et al. 1997)

and to report poor sleep quality (Arber et al. 2009), two well-known consequences of childhood abuse and predictors of MetS. Prior studies have not fully investigated the associations among gender, profile of childhood abuse, risk of developing MetS, and these two mediators.

Using biomarker data from 1,255 respondents in the 2004-2009 National Survey of Midlife Development in the U.S. (MIDUS), I investigate the effects of childhood abuse on MetS at midlife and evaluate the extent to which these patterns might be explained by two pathways: poor sleep quality and stress-induced eating. Since there are gender differences in both the nature of childhood abuse and risk of developing MetS, I conduct separate latent class analyses (LCA) for men and women. Using the classes of childhood abuse that are generated, I test the extent to which childhood abuse is associated with MetS and how poor sleep quality and stress-induced eating explain this association. Given the increasing prevalence of MetS in the U.S. and its related societal costs, understanding the mechanisms which increase risk of developing MetS may foster effective interventions and guide efficient strategies to curtail this threat to public health.

Background

Childhood Abuse and MetS for Men and Women

Over the past three decades, coronary heart disease (CHD) has been the leading cause of death in the U.S. (Jemal et al. 2005). MetS, which is made up of a cluster of risk factors including abdominal obesity, high triglycerides, low high-density lipoprotein (HDL) cholesterol, high blood pressure, and high fasting plasma glucose, is one of the main causes of CHD (Alberti et al. 2006). About 34% of U.S. adults (20 years of age and over) met the criteria for MetS in the 2003-2006 National Health and Nutrition Examination Survey (Ervin 2009). Individuals who have MetS are three to four times more likely to die of CHD and twice as likely to die from any cause compared to those without the syndrome (Lakka et al. 2002). In addition, individuals with MetS have a threefold greater risk of developing type 2 diabetes (Ford 2005). As societal costs (e.g., medical

expenditures) due to MetS have significantly increased, understanding the mechanisms that might lead to MetS is crucial to guide public health policies to decrease mortality rates in the U.S.

Stressful life events and adverse environments during childhood increase the risk for chronic diseases in adulthood (Felitti et al. 1998; Poulton et al. 2002). Multiple studies document significant associations between childhood abuse and an elevated risk of some of the components of MetS. Evidence from two prospective studies links childhood abuse to an elevated risk of being overweight and/or obese (Bentley and Widom 2009; Noll et al. 2007). For example, women who were sexually abused as children are more likely to be obese in young adulthood (ages 20-27) than non-abused women (Noll et al. 2007). Similarly, victims of childhood physical abuse, compared with non-victims, have a significantly higher body mass index (BMI) in adulthood (average age 41), even after controlling for demographic factors and risky health behaviors, such as cigarette smoking and alcohol consumption (Bentley and Widom 2009). In addition, other studies show that victims of childhood abuse are at greater risk of adult hypertension (average age 35) (Riley et al. 2010). Childhood abuse also increases risk of developing multiple metabolic risk components, such as high blood pressure, high total cholesterol, raised glycosylated hemoglobin (a form of hemoglobin that is used to identify the average plasma glucose concentration over the past two or three months), and being overweight, in both young adulthood (age 32 years) (Danese et al. 2009) and midlife (age 45 years) (Thomas et al. 2008). Some studies note that abusive (or supportive) parenting during childhood may significantly increase (or decrease) risk of developing MetS. Individuals who reported their experience of physical and psychological violence by parents during childhood are more likely to be obese at midlife, compared to those who did not report experience of such violence (Greenfield and Marks 2009). Maternal nurturance might buffer the negative impact of childhood poverty on risk of developing MetS at midlife. Among individuals who grew up in poor households, those who were raised with a high level of maternal nurturance had a lower risk of MetS, compared to those who were raised with a low level of maternal nurturance (Miller et al. 2011b).

These studies indicate that childhood abuse elevates the risk of developing MetS in adulthood, but most studies do not investigate potential mediators. Though Greenfield and Marks (2009) and Rohde et al (2008) examine stress-induced eating, binge eating, or body dissatisfaction, as mediators linking childhood abuse to obesity, this is only one of the components of MetS. Further, most studies have overlooked the importance of gender in understanding the association between childhood abuse and MetS.

Gender is a key in understanding the development of MetS. Men develop MetS at an earlier age and the prevalence of MetS is higher among men than women before women begin to enter menopause (Hwang et al. 2007). During young adulthood and early midlife, women have lower blood pressure, lower serum levels of triglycerides, and lower accumulation of abdominal fat than men. The gap between men and women narrows dramatically and even reverses beyond menopause (approximately between the ages of 40 and 60). Hormonal advantages for women, in part, contribute to a lower prevalence and later onset of MetS (Carr 2003). That is, estrogen redistributes fat away from the abdomen, which may help delay the onset of MetS for women until menopause.

Plausible Pathways Linking Childhood Abuse to MetS for Men and Women

The experience of childhood abuse may increase risk of developing MetS through psychosocial and behavioral pathways. Based on the literature related to stress, coping, and health (Contrada and Baum 2009), I consider two potential pathways: poor sleep quality and stress-induced eating.

Poor Sleep Quality. Sufficient sleep is essential to maintaining body's homeostatic functions. A clinical study of healthy young people indicates that chronic sleep deprivation disrupts carbohydrate metabolism and endocrine functions. Sleep problems, which are associated with high blood pressure, high evening cortisol concentration, and impaired glucose tolerance, may result in developing insulin resistance (Spiegel et al. 1999). A plausible biological theory is

that insufficient sleep may alter major neuroendocrine and metabolic systems by reducing leptin and elevating ghrelin levels. Low levels of leptin, an anti-starvation hormone, increase hunger, and high levels of ghrelin, a starvation hormone, increase appetite. Thus, changes in the levels of these two hormones, due to sleep problems, interrupt glucose regulation which may increase food consumption (see Klok et al. 2007 for a review of the role of leptin and ghrelin in food intake and body weight), possibly explaining why individuals who have sleep problems gain weight (Taheri et al. 2004). In contrast, reverse causality is also possible. Increased levels of inflammation due to MetS may alter sleep patterns (Imeri and Opp 2009).

A growing body of epidemiological studies supports the findings of clinical research. Sleep loss and poor sleep quality are significantly associated with high BMI in both children and adults (see Cautera et al. 2007 for a review of sleep loss and metabolic function) and with the development of MetS in adulthood (Bass and Turek 2005). Low levels of global sleep quality also significantly increase risk of developing MetS and levels of multiple MetS components (Jennings et al. 2007). Lack of sleep and difficulty sleeping through the night increase risk of developing type 2 diabetes and glucose intolerance; for example, individuals in midlife and old age who sleep less than 5 hours per night are 2.5 times more likely to have diabetes than individuals who sleep 7 hours a night (Gottlieb et al. 2005). In addition, a study finds that sleep onset latency (i.e., the amount of time it takes to fall asleep) significantly increases the levels of emotional eating scale (i.e., eating in order to deal with negative affective states in the absence of hunger) for children (Nguyen-Rodriguez et al. 2010), suggesting that children who have poor sleep habits might develop MetS in adulthood. Because most prior studies are limited to small clinical- or community-based samples, they do not control for socioeconomic status and other potential sources of stress which might partially explain associations between sleep problems and MetS components.

Victims of childhood abuse often have sleep problems. Severity of childhood abuse is significantly associated with increased risk of sleep problems in adulthood. For example, among

adults with insomnia, those who were moderately to severely abused as children report more disturbed sleep and increased nocturnal activity compared to adults who experienced minor or no abuse (Bader et al. 2007). Abused individuals might have sleep disturbances due to mental health problems, such as anxiety and/or depression (Nutt et al. 2008). Poor sleep habits, which may have originated from unstable environments in childhood, might continue in adulthood (Gregory et al. 2006), suggesting possible lingering effects of early poor sleep on MetS. Positive and significant association between adult depressive symptoms and the likelihood that an individual will develop MetS may be partially explained through physiological alterations (Kinder et al. 2004). Given the significant association between sleep problems and increased risk of developing MetS, victims of childhood abuse may be at greater risk for developing MetS than non-victims.

Gender is a significant indicator in multiple sleep domains. Men report shorter average sleep per night than women (Krueger and Friedman 2009), yet women report poorer sleep quality than men (Arber et al. 2009). Research indicates that poor sleep quality for women might be due to poor physiological and psychological conditions (e.g., depression and/or anxiety) or fluctuations in hormones across life courses (Dzajaa et al. 2005). Family demands, such as their role of caregiver for young children and sick family members, also influence sleep quality for women (Burgard 2011). Thus, investigating how sleep problems explain the association between childhood abuse and risk of developing MetS is important, given the association between sleep quality and MetS.

Stress-Induced Eating. Individuals who binge-eat often consume high-fat and high-sugar foods or eat more food than usual when they faced with stressful situations (Torres and Nowson 2007). These unhealthy eating patterns may be particularly important in understanding why victims of childhood abuse are at greater risk of developing MetS. The evidence shows that abused children, compared to those who did not experience abuse, are more likely to become "emotional eaters," a habit which might continue into adulthood (Kent et al. 1999). In addition,

women, compared to men, are more likely to be emotional eaters and to have eating problems (Tanofsky et al. 1997).

Childhood adversities may prompt the Hypothalamic Pituitary Adrenal (HPA) axis to secrete increased levels of the stress hormone cortisol, which in turn contributes to the desire for food consumption. For instance, early life trauma affects the regulation of the HPA axis hormones, including cortisol secretion from the adrenal cortex (Miller et al. 2007), and individuals with a high cortisol level, compared to those with a low cortisol level, have significantly increased desire for sweet foods and tend to consume more calories on stressful days (Epel et al. 2001). Researchers also note that individuals may fail to distinguish between anxiety and hunger (O'Connor and Conner 2009), which may lead to stress-induced obesity.

The nature of childhood abuse may determine the long-term effects of childhood abuse on binge eating (i.e., eating episodes in which the person eats an unusual amount of food without perceived control). Abused individuals with binge eating problems are more likely to develop and/or maintain obesity. Several clinical studies find that significant positive associations between sexual abuse and binge eating, and the causal association might be partially explained through mood disorder, behavioral impulsivity, and/or body image disturbance (Gustafson and Sarwer 2004). Thus, eating problems might mediate the association between childhood abuse and adult obesity. Some studies, however, have yielded contrasting results. For example, one study finds that stress-induced eating problems mediate the association between family violence in childhood and obesity in midlife (Greenfield and Marks 2009), but another finds that binge eating does not significantly mediate the association between childhood sexual/physical abuse and obesity for middle-aged women (Rohdea et al. 2008).

Some abused individuals may consciously or unconsciously decide to eat more food. Research reports that sexually abused women are more likely to be emotional overeaters (see Smolak and Murnen 2002 for a review of sexual abuse and eating disorders), and they often fail to develop other coping skills to replace eating behaviors in response to stressors. Victims of

sexual abuse, in particular, may consider gaining weight and damaging their physical and sexual attractiveness as a way to avoid additional unwanted sexual contact (Wenninger and Heiman 1998). In addition, research suggests that victims of physical abuse may increase their body size and gain weight to protect themselves from physical threats (Bentley and Widom 2009). Binge eating, whether it is an emotional coping behavior or an attempt to achieve poor body image to deflect future abuse, may lead to obesity, which in turn leads to increased risk of developing MetS in adulthood.

To summarize, there are three reasons why gender helps to more fully explain the association between childhood abuse and MetS. First, gender influences the types of abuse that children will experience; for example, girls, compared to boys, are more likely to experience sexual abuse (Sedlak et al. 2010), which is strongly associated with eating disorders (Smolak and Murnen 2002). Second, due to differences in hormonal secretion (e.g., estrogen), women have a lower risk of developing MetS prior to menopause (Carr 2003). Third, gender influences how individuals cope with experience of childhood abuse; for example, binge eating and poor sleep quality are more common in women than men (Arber et al. 2009; Grunberg and Straub 1992). Therefore, depending on their gender, children who are abused may develop MetS via different pathways.

On the basis of stress, coping, and health theories, and existing evidence, I posit and test four hypotheses:

Hypothesis 1. Men and women will have different profiles (types, frequencies, and severities) of childhood abuse.

Hypothesis 2. Severe childhood abuse will be associated with an increased risk of developing MetS for both men and women. The greater the severity of abuse, the higher the risk.

Hypothesis 3. For both men and women, childhood abuse will be associated with

poor sleep quality and eating problems. The greater severity of abuse, the greater

the extent of these problems.

Hypothesis 4. For men and women, poor sleep quality and/or eating problems

will mediate the association between childhood abuse and MetS.

Data and Methods

Sample

The sample for my study (n = 1,255) comes from two subsamples of the Midlife

Development in the United States (MIDUS) biomarker study: one from the respondents who

participated in both MIDUS I (1995-1996) and MIDUS II (2004-2005) surveys, and the other

from a supplementary sample of African Americans from Milwaukee, Wisconsin (2004-2005),

called the Milwaukee sample. The data for the biomarker study came from a two-day data-

collection protocol at the General Clinical Research Center (GCRC). The data were collected

between 2004 and 2009. Participants stayed overnight at the GCRC and completed the protocol

with a clinician. This special module includes diverse biomarkers and a detailed medical history

as well as more comprehensive questions regarding childhood abuse than those in MIDUS I. The

data collection for MIDUS was approved by the Health Sciences Institutional Review Board at

the University of Wisconsin-Madison.

MIDUS is a national study of health and aging among U.S. residents, aged 25 to 74 (b.

1920-1970), who were first interviewed between 1995 and 1996 (n = 7,108). The baseline study

included a national sample, which was obtained through random digit dialing (RDD), and

consists of respondents, siblings of many respondents (13% of the MIDUS I sample), and a

national sample of twins (24% of the MIDUS I sample) of the same age range as the national

RDD sample. Respondents were limited to only English speaking, non-institutionalized adults. A

longitudinal follow-up of the MIDUS sample was conducted 10 years after the baseline

assessment (2004-2005). At that point, a supplemental sample of 592 African Americans from Milwaukee, Wisconsin was recruited in order to investigate health in a highly segregated U.S. city. MIDUS II assessed a wide array of psychological constructs and demographic characteristics as well as extensive health measures. Based on the primary survey, four additional projects (Daily Diary Study, Cognitive Function, Bioindicators, and Neuroscience) were conducted to explore the biopsychosocial pathways to various health outcomes (Love et al. 2010).

Of those who initially responded to the questions in MIDUS I, 70% were interviewed in MIDUS II, and 21% of MIDUS II sample (n = 1,054) and 39% of Milwaukee sample (n = 201) attended the clinical examination, resulting in a total of 1,255 respondents. Compared to the respondents in the primary national sample (MIDUS I), those in this subsample had higher levels of education and personal income, visited doctors more frequently, and maintained an overall healthier life style (e.g. non-smokers). They were, however, similar to the other respondents in terms of other demographic (e.g., age, gender, and marital status) and health characteristics (for a more detailed description of the study, consult Love et al. 2010).

Measures

Dependent Variables. MetS is based on the world-wide definition established by the International Diabetes Federation (IDF) (Alberti et al. 2006). To qualify for the condition, individuals must exhibit abdominal obesity (waist circumference ≥ 94 cm for men and ≥ 80 cm for women, or BMI $\geq 30 \text{kg/m}^2$) plus at least two of the following four components: 1) elevated blood pressure (systolic pressure ≥ 130, diastolic pressure ≥ 85 or a previous diagnosis of hypertension), 2) raised triglyceride level ($\geq 1.7 \text{mmol/L}$), 3) raised glycosylated hemoglobin level (≥ 6.0 %) or previously diagnosed type 2 diabetes (see note 1), and 4) reduced high-lipoprotein ($< 40 \text{mg/dL}$ for men and < 50 mg/dL for women). During GCRC visits, medical professionals evaluated whether MIDUS participants exhibited any of the MetS components (see, Love et al. 2010 for details). Based on the IDF MetS high risk cutoffs, I create two outcome variables: MetS diagnosis and MetS components. MetS diagnosis is a dichotomous measure

reflecting whether the participant meets the IDF definition of MetS. The measure of MetS components, which ranges from 0 to 5, is a summary index of the five MetS risk factors for which each participant meets the clinical cutoffs. These two measures are used in manner consistent with a prior study (Miller et al. 2011b). Given the gender difference in risk of developing MetS in midlife, using two measures will allow me to better evaluate both the prevalence and the severity of MetS.

Independent Variables. Childhood abuse history. Childhood abuse is used as a key indicator of traumatic stress during childhood. The Childhood Trauma Questionnaire (CTQ; Bernstein and Fink 1998) is used to evaluate the severity of physical, emotional, and sexual abuse up to the age of 16. The CTQ is a well-validated measure that contains five-item subscales to assess each of the three different types of abuse (emotional, physical, and sexual abuse) and two different types of neglect (emotional and physical). It also includes a three-item scale for minimization and denial to identify respondents who are more likely to underreport negative events in childhood (e.g., "I had the best family in the world"). Respondents answered questions about childhood abuse/neglect and minimization/denial, which were measured on a scale ranging from 1 = "never true" to 5 = "very often true." The analyses are based on the 15 CTQ items that assess the three types of abuse and on the composite score from the 3 minimization/denial items (for details on the individual items of childhood abuse, see Table A2-1 in the Appendix). A composite score of each domain of childhood abuse ranges from 5 (no abuse) to 25 (extremely abuse). Latent class analysis (LCA) was used to create profiles of childhood abuse for men and women, separately, by) (for details, see "Analytic Strategy" and "Results" about LCA).

Psychosocial and Behavioral Mediators. Sleep Quality. The Pittsburgh Sleep Quality Inventory (Buysse et al. 1989), which is one of the most widely used subjective sleep quality scales based on respondents' self-reports, is used to evaluate sleep difficulties. It includes seven sleep components: 1) subjective sleep quality, 2) sleep latency, 3) sleep duration, 4) habitual sleep efficiency, 5) sleep disturbance, 6) use of sleep medications, and 7) daytime dysfunction.

Responses to items for each component range from 0 to 3, with higher scores indicating poorer

subjective sleep quality. Consistent with prior studies related to sleep and MetS (Jennings et al.

2007), I use a summary index of the seven sleep components as a measure of sleep quality,

ranging from 0 to 21. *Stress-induced eating (eating problems).* The MIDUS II included nine out

of the fifteen subscales from the COPE inventory (see Carver et al. 1989 for details), which was

developed to assess a broad range of coping responses. I use one out of the nine subscales, using

food to cope, to evaluate the participants' eating problems in response to "a stressful event". Each

respondent was asked to indicate, on a scale of one to four, how true the following two statements

are: "I eat more than I usually do" and "I eat more of my favorite foods to make myself feel

better." The possible responses were (1) a lot, (2) a medium amount, (3) only a little, and (4) not

at all. The correlation of these two indicators is .79. I reverse-code of these four responses to

generate the eating problems, which are a maximum score of the two questions, with a higher

summary score indicate more severe eating problems. I confirm that different operationalization

of measures of eating problems (using a sum of the two questions or a mean of the two questions)

do not affect findings in this study.

> *Control Variables.* In order to eliminate a spurious association between childhood abuse

and MetS due to confounding variables, this study includes five sets of covariates based on prior

studies: demographic characteristics (Johnston and Lee 2011), childhood environments (Cohen et

al. 2010), history of parents' illnesses (Lee et al. 2005), respondents' socioeconomic status

(Goldman et al. 2011), and medications (Danese et al. 2009). Childhood environments are

included to distinguish the effect of childhood abuse from other adverse childhood experiences

(Felitti et al. 1998).

> Demographic variables include gender (1 = female), race/ethnicity (white/non-white), age

of respondents at the time of MIDUS II (34-84 years old) as a linear covariate, and current marital

status at the time of the Bioindicators assessment (married/cohabiting = 1 vs. separated, divorced,

widowed, or never married = 0). SES includes the participants' educational attainment (less than

high school [reference], high school, college, more than masters' degree). For the childhood

contexts, I use the highest level of education held by a parent (less than high school [reference],

high school, more than high school), whether the respondents lived with both their biological

parents until the age of 16 (yes/no), and whether the family was on welfare or Aid to Dependent

Children (ADC) during childhood (yes/no).

To operationalize history of parents' illnesses, I create a scale ranging from 0 to 6, with 1

point being added if either of the respondent's biological parents has a history of the following

cardiovascular or MetS-related diseases: 1) heart disease, 2) high blood pressure, 3) high

cholesterol, 4) circulation problems, 5) stroke, and 6) diabetes. If a respondent does not know the

illness history of their biological parents, this is coded as 0. I confirm there is no significant

curvilinear relation between age and MetS diagnosis and components. I also include the use of

two types of medication by the respondent as inventoried by the staff of GCRC: blood pressure

medication (yes/no) and cholesterol lowering-medication (yes/no).

Analytic Strategy

Analyses are carried out in two stages: 1) LCA of childhood abuse and 2) multivariate

analyses of MetS using the groups generated by LCA. In the first stage, I determine distinctive

groups of childhood abuse. Most abused children experience multiple types of abuse with varying

degrees of severity, frequency, and chronicity (Irving and Ferraro 2006). Given the potentially

complicated nature of childhood abuse, latent modeling is beneficial in identifying the underlying

heterogeneity of the childhood abuse experience (Noonera et al. 2010). LCA has been well-

employed to identify a set of heterogeneous subgroups based on the patterns of responses to given

observed categorical variables (Collins and Lanza 2010). I use the 15 CTQ items for the LCA

(see Appendix Table A2-1 for details). To achieve a manageable number of cells and to avoid

unacceptably sparse distributions within cells in the latent analysis data matrix, I combine the five

initial response categories of CTQ into a dichotomized response for each individual abuse item

("never" and "rarely true" equal 0, and "sometimes," "often," and "very often true" equal 1) (see

note 2). In the LCA, I add a composite score of the three items of minimization/denial as a control variable to adjust for the tendency among some respondents to exaggerate positive aspects of or denied negative experience during their childhood (Bernstein and Fink 1998).

The LCA is conducted for the combined sample of men and women. After selecting the best fitting model for the whole sample, I examine gender differences in the LCA group membership using a χ^2 test, and a nested model fit test before and after adding gender into the LCA model. As results of the tests indicate that latent classes of childhood abuse vary by gender, subsequent LCA will be conducted separately for men and women. To select the best model fit (optimal number of latent classes) in subsequent comparisons between k and $k+1$ class solutions, I use the Akaike Information Criterion (AIC), the Bayesian Information Criterion (BIC), entropy, the Lo-Mendell-Rubin Likelihood Ratio Test (LRT), and interpretability. The AIC, BIC, and LRT are well-established indicators for comparing competing models (Collins and Lanza 2010; Lo et al. 2001).

Regarding the labeling of LCA classes, I use the cutoff scores recommend in the CTQ manual (Bernstein and Fink 1998) and the pattern of item response probabilities produced by LCA (see note 3 for cutoff scores and see Tables 2-1 and 2-2 for the scores of each domain across LCA classes for women and men, respectively). After determining latent classes of childhood abuse in men and women, I first conduct bivariate analyses, using F- tests and χ^2-tests, to identify whether the generated groups differ on potential mediators, outcomes, or controls.

In the second stage, using the groups generated by the LCA, I test the associations between the diverse profiles of childhood abuse and risk of developing MetS. First, multivariate ordinary least squares (OLS) and logistic regression techniques are used to determine the associations between childhood abuse and two measures of MetS: MetS diagnosis and MetS components ($M = 2.40$, $SD = 1.35$, skewness = .04), respectively, after adjusting for covariates. In the regression analyses, the latent class is entered into the models as a series of dummy variables, with the reference group comprising respondents who did not experience childhood abuse.

Second, I test the effects of potential mediators (Baron and Kenny 1986), examining the extent to which poor sleep quality and eating problems account for the associations between childhood abuse and MetS (diagnosis and components). To evaluate the significance of these mediating links, I use a binary mediation test and a Sobel test (Sobel 1982), depending on the characteristics of the outcome variables.

The percentage of missing data is approximately 13 percent when listwise deletion is applied. I impute the missing data under the missing-at-random (MAR) assumption (Allison 2001) to alleviate the potential statistical power issues in subsequent analyses. All variables except the dependent variables are included in the imputation procedure. The analyses are carried out using Mplus 6.0 (Muthén and Muthén 2008; Muthén and Muthén 2010) and STATA 11.0 (STATA Corp, 2010). To correct intra-class correlation due to some respondents from the same family (e.g., twins or siblings, 12.6% in the biomarker study), I apply robust standard error estimation.

Results

Latent Classes of Childhood Abuse and Their Characteristics among Men and Women

I find that men and women have different profiles of childhood abuse. In the combined sample of men and women, the LCA results show that a five-class solution fits the data the best. The results of gender by the LCA group χ^2 test ($p < .001$) and the model fit test in the LCA model ($p < .05$) indicate gender differences in group memberships. Thus, subsequent LCA is conducted separately for men and women, which results in a five-class solution for women and a four-class solution for men (see Appendix Table A2-1 for the results of fit indices).

[Figure 2-1 about here]

The patterns of results for each of the five classes for women and the four classes for men are displayed in Figures 2-1 and 2-2, respectively. In both figures, the y-axis indicates the item response probabilities (the proportion of responding "sometimes," "often," or "very often true" vs. "never" or "rarely true" to each of the 15 CTQ items), and the x-axis indicates the individual

CTQ items with abbreviations (see Appendix Table A2-1 for full descriptions of each item). In the legend, the size of each class (n) and the latent class probabilities (%) are reported.

[Figure 2-2 about here]

Figure 2-1 displays the five classes for women are labeled as: $Class1_{(w)omen}$ = no abuse (58.5%, n = 417); $Class2_w$ = low emotional abuse (EA)/physical abuse (PA)/sexual abuse (SA) (18.4%, n = 131); $Class3_w$ = low EA/PA/high SA (10.5%, n = 75); $Class4_w$ = high EA/PA/low SA (4.2%, n = 30); and $Class5_w$ = high EA/PA/SA (8.4%, n = 60). Similarly, Figure 2-2 shows the four classes for men are labeled as: $Class1_{(m)en}$ = no abuse (74.2%, n = 402); $Class2_m$ = low EA/ no PA/SA (16.2%, n = 88); $Class3_m$ = medium EA/ high PA/low SA (6.3%, n = 34); and $Class4_m$ = medium EA/ PA/high SA (3.3%, n = 18).

Gender differences in childhood profiles emerge in several ways. Women (41.5%) are more likely to report experiences of childhood abuse than men (25.8%). Among abused individuals, PA and EA are common for both men and women, yet women are more likely than men to report high emotional abuse. SA is also more common for women than men. For women, there are two different forms of sexual abuse: 1) high SA with other types of high abuse and 2) high SA with other types of low abuse. For men, there is only single form of SA, which occurs along with medium EA/PA. Since men and women have different profiles of childhood abuse, in the following sections, I apply all analyses for men and women, separately.

[Table 2-1 about here]

Table 2-1 and Table 2-2 display the characteristics of the latent classes of childhood abuse for women and men, respectively. Overall, both men and women who experienced abuse as children come from disadvantaged backgrounds and have more health problems than those who did not experience such abuse. For example, both men and women who experienced childhood abuse were less likely to have lived with their biological parent(s) up until the age of 16, and their families were more likely to have received welfare or ADC. Abused men are less likely than non-

abused men to have been married or cohabiting. Abused women are more likely to have taken blood pressure medication.

[Table 2-2 about here]

Associations between Childhood Abuse and MetS among Women

Rows 3 to 4 in Table 2-3 show adjusted probability of being diagnosed with MetS and adjusted mean of the number of MetS components, respectively, across female childhood abuse groups. I find that women who experienced all types of high abuse have a greater risk of developing MetS and a higher number of MetS components, compared to non-abused women and some of other abused women. Specifically, women with high EA/PA/SA (Class5_w = 66 %) have a greater risk of developing MetS than non-abused women (Class1_w = 38 %) and than women in other two abuse groups (Class2_w = 39 % and Class3_w = 44 %). Similarly, women with high EA/PA/SA (Class5_w = 2.7) have significantly higher levels of MetS components than non-abused women (Class1_w = 2.3) and women in the other abuse group (Class2_w = 2.2). Therefore, in the following mediation model for women, I use both MetS diagnosis and MetS components.

Associations between Childhood Abuse and MetS among Men

Rows 12 to 13 in Table 2-3 show adjusted probability of MetS diagnosis and adjusted mean of the number of MetS components, respectively, across male childhood abuse groups. I find that men who experienced medium EA/high PA with low SA have a higher number of MetS components, than non-abuse men. The experience of high SA, however, is not necessarily associated with an increased risk of MetS diagnosis and elevated number of MetS components. Specifically, men with a history of medium EA/high PA/low SA are likely to have higher levels of MetS components than non-abused men (Class3_m = 3.1 vs. Class1_m = 2.5), which is statistically different (p <. 05). There is no significant difference in the number of MetS components between men in no-abuse group (Class1_m) and men in the other abuse groups (Class2_m and Class4_m). In addition, there is no significant difference in risk of MetS diagnosis across male childhood abuse

groups. Therefore, in the following mediation model for men, I use MetS components as an outcome variable in comparison between men in $Class1_m$ and $Class3_m$.

Associations between Childhood Abuse and Poor Sleep Quality and Stress-Induced Eating among Women

Rows 6 to 7 in Table 2-3 show adjusted means of poor sleep and eating problems, respectively, across female childhood abuse groups. I find that some of the abused women have increased levels of both poor sleep and eating problems. While severity of childhood abuse is positively associated with sleep problems, it is not necessarily related to eating problems.

Specifically, most abused women are more likely than non-abused women to have higher levels of sleep problems. In particular, women who experienced all types of high abuse ($Class5_w$ = 8.8) are more likely to have significantly higher levels of sleep problems than other types of abused women in $Class2_w$ (= 7.3) and $Class3_w$ (= 7.0). Yet, there is no significant difference in levels of sleep problems between women in $Class5_w$ and those in $Class4_w$ (= 7.2). Regarding eating problems, women who experienced low EA/PA/SA ($Class2_w$ = 2.4) have significantly higher levels of eating problems than non-abused women ($Class1_w$ = 2.2). Yet, there is no significant difference in levels of eating problems between non-abused women and women in other abuse groups, including women in high EA/PA/SA ($Class5_w$ = 2.5).

Associations between Childhood Abuse and Poor Sleep Quality and Stress-Induced Eating Problems among Men

Rows 14 to 15 in Table2-3 show the adjusted means of poor sleep and eating problems, respectively, across male childhood abuse groups. The experience of childhood abuse is significantly associated with both sleep and eating problems for men. Most abused men have higher levels of sleep problems than non-abused men, yet experience of childhood abuse is not necessarily related to eating problems.

Compared to non-abused men ($Class1_m$ = 5.5), some abused men ($Class3_m$ = 7.2 and $Class4_m$ = 7.8) are more likely to have sleep problems. There are, however, no significant

differences in levels of sleep problems between non-abused men and men in Class2$_m$ (= 6.2).

Regarding eating problems, compared to non-abused men (Class1$_m$ = 1.7), some abused men

(Class2$_m$ = 2.2 and Class3$_m$ = 2.0) are likely to have greater eating problems. Interestingly, men

who experienced medium EA/PA with high SA (Class4$_m$ = 1.7) have lower levels of eating

problems than men in other abuse groups, and there is no difference in levels of eating problems

between men in Class4$_m$ and non-abused men.

[Table 2-3 about here]

Poor Sleep Quality and Eating Problems as Mediators of Childhood Abuse and MetS for Women

Columns 3 to 5 in Table 2-4 show the results of the mediation model for MetS diagnosis

among women. I find that sleep and eating problems are significantly associated with risk of

developing MetS for women. Yet, these were no significant mediation effects of these two factors

to explain why women who experienced all types of high abuse are at greater risk of developing

MetS than non-abused women.

Specifically, after controlling for childhood abuse, eating problems are significantly

associated with a diagnosis of MetS, but the associations between sleep problems and MetS is not

statistically significantly. When eating problems are included in the model, the odds ratio of high

childhood abuse (Class5$_w$) decreases from 3.15 to 2.81, but the result of the mediation test is not

significant (p > .05). Regardless of including either poor sleep quality or stress-induced eating as

a mediator, high childhood abuse (Class5$_w$), compared to no abuse, has a significant effect on

MetS diagnosis, and eating problems also have a significant main effect on MetS diagnosis.

[Table 2-4 about here]

Columns 3 to 5 in Table 2-5 show the results of the mediation model for MetS

components among women. After controlling for childhood abuse, both poor sleep quality and

eating problems are significantly associated with MetS components. When sleep problems are

included as a mediator, the estimated coefficients of high childhood abuse (Class5$_w$) decrease

slightly from .42 to .34 (19% change), but the result of a Sobel test is only marginally significant (p = .051). Similarly, when stress-induced eating are included as a mediator, the estimated coefficients of Class5$_w$ drop from .42 to .35 (17% change), yet a Sobel test shows that the mediation effect is not significant (p =.11). After including childhood abuse, both sleep problems and stress-induced eating also have a significant main effect on MetS components.

[Table 2-5 about here]

Poor Sleep Quality and Eating Problems as Mediators of Childhood Abuse and MetS among Men

Columns 3 to 5 in Table 2-6 show the results of the mediation model for men. I find that problems with both sleep and eating increase the number of MetS components for men. However, these two factors do not significantly explain why men who experience medium EA/high PA and low SA (Class3$_m$) have higher number of MetS components than non-abused men. Specifically, eating problems and poor sleep quality significantly predict a number of MetS components. When sleep quality is included into the model, the coefficient of Class3$_m$ decreases slightly from .53 to .47 (11% change); when eating problems are included in the model, the coefficient decreases in same magnitude. The results of a Sobel test show that both sleep quality (p = .07) and eating problems (p =.08) do not significantly mediate the effect of such childhood abuse on MetS components. Even after including either poor sleep quality or eating problems, childhood abuse still predicts an increased number of MetS components.

[Table 2-6 about here]

Discussion

In this article, I test whether men and women experience different profiles of childhood abuse, whether each profile is associated with a distinct level of risk for developing MetS, and whether two potential mediators (poor sleep quality and stress-induced eating) explain the association between childhood abuse and risk of developing MetS in men and women. Several key contributions emerge in my findings. First, I find that men and women have different profiles

of childhood abuse. Women have five categories of childhood abuse, while men have four. Sexual abuse is more common for women than men across profiles; although both men and women experience physical and emotional abuse, the likelihood of experiencing each type of abuse varies by gender. For women, there are two profiles that include sexual abuse. In the first profile, all three types of abuse are highly prevalent and severe, and in the other second, sexual abuse is highly prevalent and severe, but there are low levels of emotional and physical abuse. For men, the one profile that includes sexual abuse includes medium emotional and physical abuse. My findings are consistent with prior studies, indicating a higher incidence of sexual abuse for women (Sedlak et al. 2010), but I extend previous research by revealing complicated profiles of childhood abuse.

My second contribution involves identifying the association between the experience of childhood abuse and risk of developing MetS. I find that some abused individuals have an increased risk of developing MetS, which is somewhat consistent with research that documents an association between childhood abuse and increased risk of developing MetS (Danese et al. 2009), obesity, and/or type 2 diabetes (Bentley and Widom 2009; Greenfield and Marks 2009; Rohdea et al. 2008; Thomas et al. 2008). While most prior research, except Danese et al. (2009), has used a single component of MetS (e.g., obesity or a higher BMI), my study uses a comprehensive measure of MetS, following the International Diabetes Federation's definition. In addition, while most prior studies have used single categories of childhood abuse (usually sexual or physical) that are often defined narrowly, I show that complex categories of childhood abuse, each characterized by distinct likelihoods of experiencing different types of abuse, affect risk of developing MetS. That is, not all abused individuals are at greater risk of developing MetS. While women who experienced all types of high abuse are more likely to have MetS than non-abused women, I find that only men who experienced high physical and medium emotional abuse have a greater number of MetS components. The literature shows that women who experienced sexual abuse are more likely to develop chronic diseases than those who were not sexually abused.

Sexual abuse often leads to self-blaming and stigmatization among women, which in turn shapes overall health consequences in multiple ways, possibly leading to mental health problems (Kendler et al. 2000) and eating disorders (Smolak and Murnen 2002). These consequences might be one of reasons why sexual abuse is an important contributor to women's risk of developing MetS.

In the association between childhood abuse and two potential mediators (poor sleep quality and eating problems) I find that childhood abuse is associated with sleep problems in adulthood. Higher frequencies of childhood abuse are associated with increased levels of sleep problems, and this pattern is similar across gender. My findings are comparable with prior research on childhood abuse poor sleep quality (Greenfield et al. 2011) and even sleep pathology (Gregory et al. 2006). However, the associations between childhood abuse and eating problems vary by class and gender; for both men and women, the frequency of childhood abuse is not necessarily associated with stress-induced eating.

Interestingly, men with a history of sexual abuse do not report higher levels of eating problems, compared to non-abused men. In supplementary analyses, I find that men who experienced sexual abuse are less likely to smoke than non-abused men. Thus, the men in this group might not adopt negative coping behaviors, such as stress-induced eating and smoking, in response to stressors. Due to the small sample size (n = 18, 3.3%) of this group, this finding does not lend itself to generalizability, but I confirm that this group appears in all LCA models (see Table A2-2 in the Appendix), indicating that the existence of this group might not be attributed to random error. Since only individuals who visited GCRC reported their experience of childhood abuse, the data might be under-reported. A previous study shows that the prevalence of self-reported sexual abuse varies by the nature of the abuse. While approximately 13% of men reported being touched or fondled in a sexual way by age 18, only about 7% of men reported experiencing forcible sexual intercourse (oral or anal) by age 18 (Dube et al. 2005). I know of very few studies that investigate the effects of sexual abuse on poor physical health outcomes for

men. Future studies should explore risk of developing MetS in a larger sample of men who experienced different types and frequencies of sexual abuse.

I find that for women, the experience of childhood sexual abuse does not always elevate risk of stress-induced eating. That is, women who experienced sexual abuse with low other types of abuse report lower levels of eating problems, compared to women in the other abuse groups. The literature documents that women who experienced sexual abuse often tend to exhibit different eating disorders (binge eating, bulimia nervosa, or anorexia). Women in this group might have anorexia rather than binge eating. In addition, weight stigmatization for women might be another factor explaining why some women who experienced sexual abuse as children do not always gain weight (Friedman et al. 2005b). Future research should explore the role of sexual abuse on various types of eating problems and their effects on MetS onset for women.

The associations between childhood abuse and MetS become less significant when eating problems and poor sleep quality are included into the model. This suggests that these two mediators, to some extent, might help explain why individuals who experienced childhood abuse have an increased risk of developing MetS. Yet, the mediation effects are not statistically significant, which might be partially attributed to a lack of statistical power, possibly due the small sample size. In addition, approximately 23% of women in the sample are pre-menopausal (average age of 42), which suggests that the secretion of estrogen may help to delay the onset of MetS. Future follow ups of this sample will shed more light on this issue.

The fact that childhood abuse still significantly predicts the likelihood of developing MetS after controlling for the two mediators indicates there are other unexplained mechanisms. Genetic and early environmental factors might affect risk of developing MetS. According to biological programming theory, malnutrition during gestation and low birth weight predict risk of developing diabetes in adulthood (Barker 1990). Accelerated growth in infancy, in particular for infants born with low birth weight, gives rise to metabolic discontinuity and possibly increases risk of developing MetS in adulthood (Ferraro and Shippee 2009). Social, behavioral, and

emotional factors might affect the risk of developing diseases related to MetS. For example, insufficient social skills and support (Suarez et al. 1998), physical inactivity and unhealthy dietary habits (Park et al. 2003), and depressive symptoms (Lett et al. 2004) are also known as risk factors of developing MetS. All these factors are more common for victims of childhood abuse than non-victims. Furthermore, there may be other male-typed maladaptive coping strategies (e.g., heavy drinking and unhealthy eating) that link childhood abuse to risk of developing MetS. Future research needs to consider these possibilities.

Limitations and Future Directions

My study is not without limitations. First, given the cross-sectional nature of the biomarker data, it is not possible to definitively ascertain causal ordering between mediators and MetS. Studies indicate that individuals who have MetS are more likely to have sleep problems (Foley et al. 2004). Individuals who have type 2 diabetes have an increased desire for food intake (Liese et al. 2009), which might cause them to overeat. Thus, from the evidence here, I infer that childhood abuse influences the chances that an individual will develop MetS. To better understand the causal pathways, future studies should explore mediation effects with prospective data collected at various times throughout childhood and adulthood.

In addition, there might be a recall bias in reporting childhood abuse since questions about abuse were asked in midlife. As previous studies point out, there exists the possibility that individuals with mood disorders might exaggerate or misrepresent their adversities during childhood (White et al. 2007; Widom and Morris 1997). Nonetheless, recent studies report that memories of specific childhood experiences are highly stable (Yancura and Aldwin 2009), and delayed recollection of traumatic memories, such as childhood abuse, tends to be fairly accurate (Hardt and Rutter 2004). In supplementary analyses, I also find strong correlation and consistency between reports of physical abuse at MIDUS I and MIDUS II (correlation = .76 and Cohen's kappa = 84.5%). Given the use of slightly different measures (Conflict Tactics Inventory in MIDUS I and CTQ in MIDUS II) that were collected 10 years apart, the measures of self-

reported childhood abuse in this study appear quite reliable. In addition, research on individuals' appraisals of stressful events and the various coping strategies used to deal with them has pointed out the importance of considering an individual's subjective perception of stressors (Lazarus and Folkman 1984). That is, the way that victims of childhood abuse assess the adversity of early life events might explain whether they adopt negative or positive coping strategies and their concomitant health consequences.

Third, the sample size of this study (n = 698 for women and n = 535 for men) is relatively small to adequately apply LCA to the complete 25 CTQ items (15 items of childhood abuse and 10 items of neglect). To avoid unacceptable sparse distributions within statistical cells in the LCA data matrix, my analyses do not include childhood neglect items (10 CTQ items). Many studies find that parental neglect during childhood is significantly associated with obesity in adulthood (Johnson et al. 2002; Lissau and Sorensen 1994; Thomas et al. 2008). Long-term neglect might lead to unhealthy eating behaviors and physical inactivity, which might contribute to risk of developing MetS in adulthood. Thus, future studies should use a broader concept of childhood abuse and neglect and test its effect on MetS in a large sample.

Finally, researchers should be careful when they apply my findings to the general population. Respondents in this study were individuals who agreed to visit clinical settings for the survey of this special biomarker module, and they might be located in the areas close to the GCRC. The participants who are mentally and physically unhealthy might not have been able to visit GCRC. Thus, sampling selection might be biased. In addition, these respondents reported higher levels of education compared to the respondents who did not participate in this biomarker study. Given the higher prevalence of childhood abuse among people who have low SES, I might underestimate the associations between childhood abuse and risk of developing MetS. Future studies should replicate this study using larger population-based data.

Despite these limitations, there is much to be learned from my findings that will contribute to the existing literature. Many abused survivors do not develop MetS, and many

people who are not abused develop MetS. This indicates the experience of childhood abuse is not able to fully explain risk of developing MetS, but obviously there is a significant link. Risk of developing MetS is higher for children who experience high levels of abuse than for those who are not abused. Thus, I propose that public intervention programs be developed that help the victims of childhood abuse to achieve healthy behaviors that may prevent the onset of MetS. Intervention programs need to be designed that adequately address gender differences in the nature of early life adversity, coping resources and strategies, and the prevalence of chronic diseases. Such interventions will ultimately reduce the downstream societal costs of childhood abuse.

Notes

1. Raised fasting-glucose levels (i.e., ≥ 5.6 mmol/L) is one of criteria of metabolic syndrome defined IDF. Since this variable has not been publicly released yet, I use glycosylated hemoglobin (HbA1c) (i.e., $\geq 6.0\%$), instead. Glycosylated hemoglobin is an indicator of glucose regulation over the past two or three months, which can be used as an indicator of pre-diabetic condition, initial diabetes screening, and diabetic control (Rohlfing et al. 2000).

2. I treat the frequency of experiencing each CTQ item equally (1 = sometimes, often, very often true vs. 0 = never and rarely true). Across the 15 CTQ items, I acknowledge that some (e.g., "I felt that someone in my family hated me") reflect less severe forms of abuse than others (e.g., "Someone tried to make me do sexual things or watch sexual things"). As such, the effect of some forms of abuse (e.g., emotional) might be less harmful than the effect of other forms of abuse (e.g., sexual) in terms of influencing risk of developing MetS.

3. The CTQ manual provides the following cutoff scores for each type of abuse: 1) emotional abuse: no (5-8), low (9-12), medium (13-15), and high (16-25); 2) physical abuse: no (5-7), low (8-9), medium (10-12), and high (13-25); and 3) sexual abuse: no (5), low (6-7), medium (8-12), and high (13-25).

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Table 2-1 Bivariate Analysis, by Latent Class of Childhood Abuse for Women (n = 698)

Childhood Abuse Classes for Women[a,c]	Total n = 698		Class1$_w$ n = 408		Class2$_w$ n = 129		Class3$_w$ n = 74		Class4$_w$ n = 29		Class5$_w$ n = 58		χ^2 (df) F-tests
	Mean/ %	SD	Mean/ %	SD	Mean/ %	SD	Mean/ %	SD	Mean/ %	SD	Mean/ %	SD	
Age (34-84)	54.2	11.5	55.4	11.6	52.3	11.6	54.6	11.4	51.1	10.8	50.0	10.2	4.2 (4)**
White	76		78		75		70		82		60		11.1 (4)*
Married/cohabitating	56		59		51		64		55		45		6.9 (4)
SES													
≤ High school	30		30		29		35		41		38		11.5 (12)
Some college	21		21		16		19		10		22		
College degree	26		26		33		26		38		24		
≥ Master degree	23		23		22		20		10		16		
Parents' education													
Less than high school	24		24		36		24		24		41		15.4 (8)
High school	30		31		30		38		38		33		
More than high school	45		45		34		38		38		26		
Living with parents until age 16	81		85		78		78		83		66		13.8 (4)**
Family on welfare in childhood	12		7		12		12		28		41		61.9(4)***
Number of parent's illness (0-6)	2.4	1.6	2.3	1.5	2.6	1.7	2.2	1.6	2.7	1.6	2.3	1.7	1.6(4)
Blood pressure medication	38		39		27		50		38		38		11.3 (4)*
Cholesterol medication	22		22		19		22		28		24		1.2 (4)
Emotional abuse (5-25)[b]	8.6	4.7	5.8	1.3	11.4	3.4	8.2	2.3	18.8	4.1	17.3	4.1	513(4)***
Physical abuse (5-25)[b]	7.0	3.2	5.7	1.0	7.0	2.0	6.7	1.8	14.1	3.7	13.4	4.1	335 (4)***
Sexual abuse (5-25)[b]	7.3	4.7	5.3	.8	5.7	1.3	14.3	4.6	5.8	1.4	18.3	4.6	649 (4)***

Note: [a]Respondents (n = 15) who have missing information for MetS indicators are excluded from bivariate analysis.

[b]5 = no abuse ~ 25 = extreme abuse

[c]Class1$_w$ = no abuse; Class2$_w$ = low EA/PA/SA; Class3$_w$ = low EA/PA/high SA; Class4$_w$ = high EA/PA/low SA; Class5$_w$ = high EA/PA/SA.

Abbreviations. $_w$ = women; EA = emotional abuse; PA = physical abuse; SA = sexual abuse.

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

Table 2-2 Bivariate Analysis, by Latent Class of Childhood Abuse for Men (n = 535)

Childhood Abuse Classes for Men[a,c]	Total n = 535		Class1$_m$ n = 399		Class2$_m$ n = 84		Class3$_m$ n = 34		Class4$_m$ n = 18		χ^2/ F-tests
	Mean/ %	SD	Mean/ %	SD	Mean/ %	SD	Mean/ %	SD	Mean/ %	SD	
Age (34-84)	55.1	11.9	56.4	12.4	51.1	9.6	51.3	8.9	53.7	10.9	6.0 (4)**
White	83		85		75		82		78		5.7 (3)
Married/cohabitating	76		79		61		82		67		14.6 (3)**
SES											
≤ High school	24		23		29		29		17		5.1 (9)
Some college	15		14		17		18		22		
College degree	38		39		36		38		33		
≥ Master degree	23		24		19		15		28		
Parents' education											
Less than high school	24		24		19		21		55		12.1 (6)
High school	38		37		38		44		28		
More than high school	39		39		43		35		17		
Living with parents until age 16	73		76		67		56		56		11.5 (3)**
Family on welfare in childhood	6		4		12		6		11		8.4 (3)*
Number of Parent's history of illnesses (0-6)	2.0	1.4	2.0	1.5	2.1	1.5	1.7	1.3	2.11	1.4	.8
Blood pressure medication	34		34		40		26		28		2.7
Cholesterol medication	35		38		24		29		33		7.0 (3)
Emotional abuse (5-25)[b]	7.3	3.4	5.8	1.2	10.5	2.5	13.3	4.6	13.9	5.3	307.1(3)***
Physical abuse (5-25)[b]	6.9	2.7	6.1	1.2	7.3	1.7	14.1	3.4	11.1	5.3	259.8 (3)***
Sexual abuse (5-25)[b]	5.6	2.3	5.2	.7	5.4	1.6	6.1	2.0	16.4	3.7	543.2 (3)***

Note: [a]Respondents (n = 7) who have missing information for MetS indicators are excluded from bivariate analysis.

[b]5 = no abuse ~ 25 = extreme abuse.

[c]Class1$_m$ = no abuse; Class2$_m$ = low EA/no PA/SA; Class3$_m$ = medium EA/high PA/low SA; Class4$_m$ = medium EA/PA/high SA.

Abbreviations. $_m$ = men; EA = emotional abuse; PA = physical abuse; SA = sexual abuse.

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

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Table 2-3 Adjusted Means or Probabilities for Dependent Variables and Mediators, by Latent Class of Childhood Abuse for Women and Men

Childhood Abuse Classes for Women (n = 698)[a,b,c]	$Class1_w$ n = 408	$Class2_w$ n = 129	$Class3_w$ n = 74	$Class4_w$ n = 29	$Class5_w$ n = 58
Adjusted probability of MetS (%)	38	39	44	49	66
Adjusted mean of MetS components, (Mean [SE])	2.3 (.7)	2.2 (.1)	2.4 (.1)	2.3 (.2)	2.7 (.2)
Adjusted mean of poor sleep quality (Mean [SE])	6.0 (.2)	7.3 (.3)	7.0 (.4)	7.2 (.6)	8.8 (.6)
Adjusted mean of eating problems (Mean [SE])	2.2 (.1)	2.4 (.1)	2.3 (.1)	2.2 (.2)	2.5 (.2)

Childhood Abuse Classes for Men (n=535)[d,e]	$Class1_m$ n = 399	$Class2_m$ n = 84	$Class3_m$ n = 34	$Class4_m$ n = 18
Adjusted probability of MetS (%)	51	55	68	49
Adjusted mean of MetS components, (Mean [SE])	2.5 (.1)	2.7 (.1)	3.1 (.2)	2.2 (.3)
Adjusted mean of poor sleep quality (Mean [SE])	5.5 (.2)	6.2 (.4)	7.2 (.6)	7.8 (.6)
Adjusted mean of eating problems (Mean [SE])	1.7 (.05)	2.2 (.1)	2.0 (.1)	1.7 (.2)

Note: [a]All control variables (demographics, childhood environments, parents' illness history, and medications) are adjusted.

[b]Respondents (n = 15) who have missing information for MetS indicators were excluded from bivariate analysis.

[c]$Class1_w$ = no abuse; $Class2_w$ = low EA/PA/SA; $Class3_w$ = low EA/PA/high SA; $Class4_w$ = high EA/PA/low SA; $Class5_w$ = high EA/PA/SA.

[d]Respondents (n = 7) who have missing information for MetS indicators are excluded from bivariate analysis.

[e]$Class1_m$ = no abuse; $Class2_m$ = low EA/no PA/SA; $Class3_m$ = medium EA/high PA/low SA; $Class4_m$ = medium EA/PA/high SA.

Abbreviations. $_w$ = women; $_m$ = men; EA = emotional abuse; PA = physical abuse; SA = sexual abuse; SE = standard error.

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

Table 2-4 Odds Ratios (95% CI) Revealing Plausible Pathways Linking Childhood Abuse and MetS Diagnosis for Women (n = 698)

		Covariate Adjusted Model	Sleep Quality Mediation Model	Eating Behavior Mediation Model
Variables[a]				
Childhood Abuse	No abuse (Class1$_w$)	1 [Reference]	1 [Reference]	1 [Reference]
	Low EA/PA/SA (Class2$_w$)	1.02 (.65-1.59)	.95 (.61-1.50)	.91 (.57-1.44)
	Low EA/ PA/High SA (Class3$_w$)	1.29 (.74-2.25)	1. 24 (.71-2.15)	1. 25 (.71-2.19)
	High EA/PA/Low SA (Class4$_w$)	1.54 (.67-3.56)	1.46 (.62-3.43)	1.52 (.63-3.66)
	High EA/PA/SA (Class5$_w$)	3.15 (1.65-6.05)**	2.81 (1.43-5.55)**	2.95 (1.52-5.72)**
Mediators	Poor sleep quality		1.04 (1.00-1.09)	
	Eating problems			1.44 (1.23-1.69)***
χ^2 (df)		101.80 (17)	104.73 (18)	105.13 (18)
χ^2 difference (df)			2.93 (1)	3.33 (1)

Note. [a]All control variables (demographics, childhood environments, parents' illness history, and medications) are adjusted for the models.
 *$p < .05$; ** $p < .01$; *** $p <.001$.
Abbreviations.$_w$ = women; EA = emotional abuse; PA = physical abuse; SA = sexual abuse; CI = confidence interval.

Table 2-5 Estimated Coefficients (SE) Revealing Pathways Linking Childhood Abuse and A Number of MetS Components among Women (n = 698)

Variables[a]		Covariate Adjusted Model (SE)	Sleep Quality Mediation Model (SE)	Eating Behavior Mediation Model (SE)
Childhood Abuse	No abuse (Class1$_w$)	1[Reference]	1[Reference]	1[Reference]
	Low EA/PA/SA (Class2$_w$)	-.05 (.13)	-.08 (.13)	.11 (.13)
	Low EA/ PA/High SA (Class3$_w$)	.11 (.16)	.08 (.15)	.09 (.15)
	High EA/PA/Low SA (Class4$_w$)	.06 (.25)	.03 (.25)	-.04(.26)
	High EA/PA/SA (Class5$_w$)	.42 (.19)*	.34 (.20)	.35 (.19)
Mediators	Poor sleep quality		.03 (.01)*	
	Eating problems			.22 (.04)**
R-squared		0.226	0.231	0.253

Note. [a]All control variables (demographics, childhood environments, parents' illness history, and medications) are adjusted.

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

Abbreviations.$_w$ = women; EA = emotional abuse; PA = physical abuse; SA = sexual abuse; SE = standard error.

Table 2-6 Estimated Coefficients (SE) Revealing Pathways Linking Childhood Abuse and the Number of MetS for Men (n = 535)

Variables[a]		Covariate Adjusted Model (SE.)	Sleep Quality Mediation Model (SE)	Eating Behavior Mediation Model (SE)
Childhood Abuse	No abuse (Class1$_m$)	1[Reference]	1[Reference]	1[Reference]
	Low EA/ No PA/SA (Class2$_m$)	.15 (.16)	.12 (.16)	.06 (.16)
	Medium EA/ High PA/Low SA (Class3$_m$)	.53 (.21)*	.47 (.21)*	.47 (.21)*
	Medium EA/PA/High SA. (Class4$_m$)	-.30 (.32)	-.39 (.33)	-.30 (.30)
Mediators	Poor sleep quality		.04(.02)*	
	Eating problems			.20 (.06)**
R-squared		0.116	0.126	0.135

Note. [a]All control variables (demographics, childhood environments, parents' illness history, and medications) are adjusted for the models.
*$p < .05$; ** $p < .01$; *** $p < .001$.
Abbreviations. $_m$ = men; EA = emotional abuse; PA = physical abuse; SA = sexual abuse; SE = standard error.

Figure 2-1 Profiles of Childhood Trauma Questionnaire (15 items) for the 5-Class Solution for Women

Probability of responding "sometimes, often, very often true" to each CTQ item

Emotional Abuse   Phyiscal Abuse   Sexual Abuse

Class1w, 58.5%, n=417   Class2w, 18.4%, n=131   Class3w, 10.5%, n=75   Class4w, 4.2%, n=30   Class5w, 8.4%, n=60
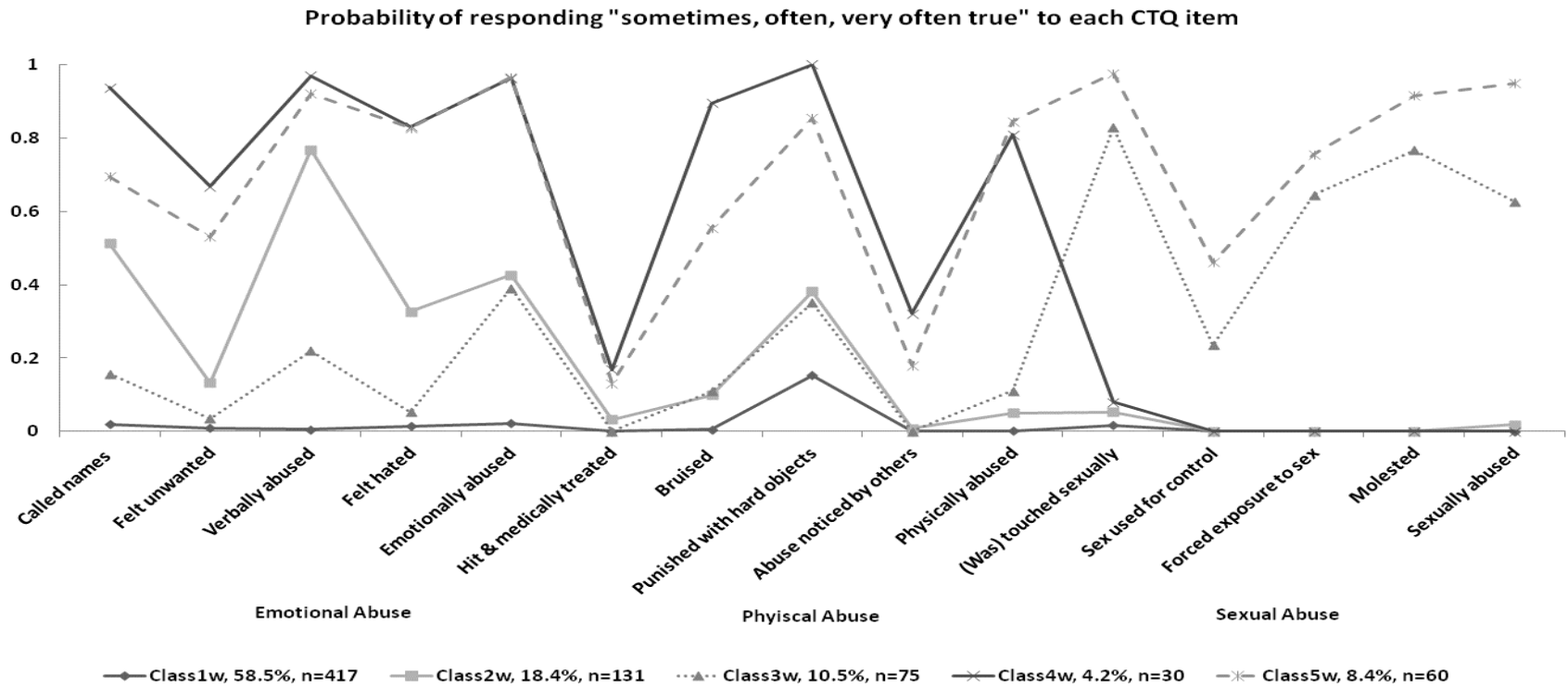
Legend. Class1$_w$ = no abuse; Class2$_w$ = low EA/PA/SA; Class3$_w$ = low EA/PA/high SA; Class4$_w$ = high EA/PA/low SA; Class5$_w$ = high EA/PA/SA.
Abbreviations. $_w$ = women; EA = emotional abuse; PA = physical abuse; SA = sexual abuse.

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Figure 2-2 Profiles of Childhood Trauma Questionnaire (15 items) for the 4-Class Solution for Men

Probability of responding "sometimes, often, very often true" to each CTQ item
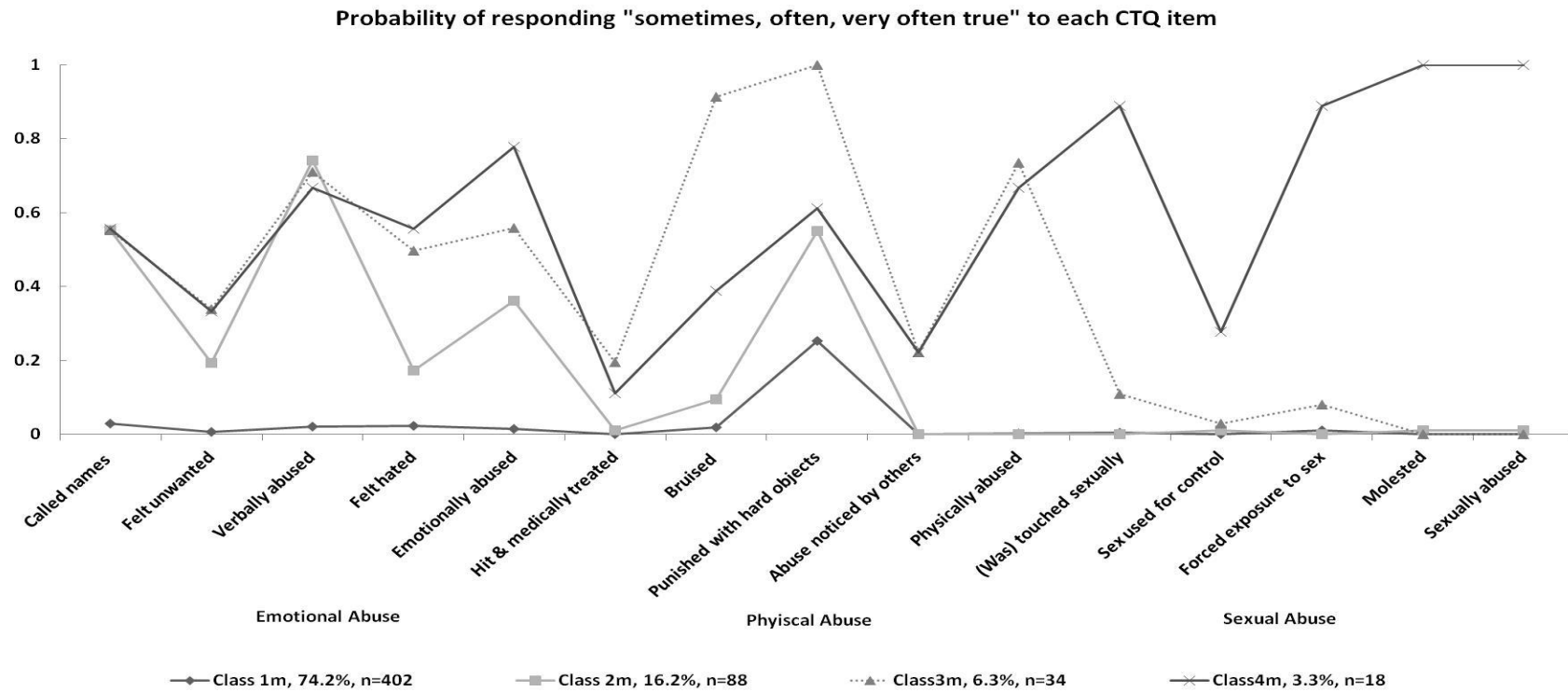
Legend. Class1ₘ = no abuse; Class2ₘ = low EA/no PA/SA; Class3ₘ = medium EA/high PA/low SA; Class4ₘ = medium EA/PA/high SA.
Abbreviations. ₘ = men; EA = emotional abuse; PA = physical abuse; SA = sexual abuse.

Appendix

Table A2-1 Childhood Trauma Questionnaire Items (CTQ) Used in the Analyses

Type of Abuse	Reliability (α)	Items	Abbreviation
Emotional	Female: .84 Male: .78	People in my family called me things like "stupid," "lazy," or "ugly."	Called names
		I thought that my parents wished I had never been born.	Felt unwanted
		People in my family said hurtful or insulting things to me.	Verbally abused
		I felt that someone in my family hated me.	Felt hated
		I believe that I was emotionally abused.	Emotionally abused
Physical	Female: .72 Male: .65	I got hit so hard by someone in my family that I had to see a doctor or go to the hospital.	Hit & medically treated
		People in my family hit me so hard that it left me with bruises or marks.	Bruised
		I was punished with a belt, a board, a cord, or some other hard object.	Punished with hard objects
		I got hit or beaten so badly that it was noticed by someone like a teacher, neighbor, or doctor.	Abuse noticed by others
		I believe that I was physically abused.	Physically abused
Sexual	Female: .92 Male: .92	Someone tried to touch me in a sexual way, or tried to make me touch them.	(Was) touched sexually
		Someone threatened to hurt me or tell lies about me unless I did something sexual with them.	Sex used for control
		Someone tried to make me do sexual things or watch sexual things.	Forced exposure to sex
		Someone molested me.	Molested
		I believe that I was sexually abused.	Sexually abused
Minimization/Denial	Female: .82 Male: .77	There was nothing I wanted to change about my family.	
		I had the perfect childhood.	
		I had the best family in the world.	

Note. A possible response is never true, rarely true, sometimes true, often true, or very often true.

Table A2-2 Fit Indices for Latent Class Model for Women and Men

		AIC[a]	BIC[a]	Entropy[d]	LRT[c]	Size of classes: n, %			
Women	Class 3	6085.12	6309.03	.94	546.04*	1: n = 124,	17.4%	2: n = 127,	17.8%
						3: n = 462,	64.8%		
	Class 4	5780.16	6081.75	.95	335.95*	1: n = 128,	18.0%	2: n = 61,	8.6%
						3: n = 75,	10.5%	4: n = 449,	63.0%
	Class 5	5636.10	6015.26	.93	176.58*	1: n = 30,	4.3%	2: n = 60,	8.5%
						3: n = 75,	10.5 %	4: n = 417,	58.6%
						5: n = 131,	18.4 %		
	Class 6	5599.96	6056.90	.91	69.4	1: n = 58 ,	8.1%	2: n = 32,	4.5%
						3: n = 75,	10.5%	4: n = 31,	4.3%
						5: n = 402,	5.6%	6: n = 115,	16.1%
Men	Class 3	3297.95	3508.42	.93	234.55*	1: n = 18,	3.3%	2: n = 97,	17.9%
						3: n = 427,	78.8%		
	Class 4	3203.92	3487.41	.91	126.84*	1: n = 402,	74.2%	2: n = 34,	6.3%
						3: n = 88,	16.2%	4: n = 18,	3.3%
	Class 5	3177.99	3534.49	.92	59.38*	1: n = 81,	14.9%	2: n = 396,	73.1%
						3: n = 18,	3.3%	4: n = 13,	2.4%
						5: n = 34,	6.3%		
	Class 6	3159.98	3589.51	.93	54.09	1: n = 396,	73.1%	2: n = 13,	2.4%
						3: n = 81,	15.0%	4: n = 10,	1.9%
						5: n = 8,	14.8%	6: n = 34,	6.3 %

Note: * *p* <.05

[a]Lower AIC and BIC values indicate better model fit.

[b]Entropy should be greater than .07; values close to 1 are better model fit.

[c]Less than .05 *p*-value of Lo-Mendell-Rubin LRT test indicates that k-1 classes are sufficient and k classes are not needed.

In addition to these indices, interpretability and theoretical expectation are important factors to determine the number of classes.

Chapter 4-Childhood Abuse and Elevated Markers of Inflammation in Adulthood: Do the Effects Differ Across Life Course Stages?

Abstract

Research indicates that victims of childhood abuse have an increased risk of developing immune-related disorders in adulthood. Elevated markers of inflammation under stressful conditions have been considered as a plausible explanation for the high prevalence of such disorders among victims. Most studies related to health disparities have focused on the effects of SES differences on health outcomes, but little research has investigated whether the effects of early life adversity on inflammatory markers vary across age groups. Guided by life course and selective mortality approaches, this study investigates the associations between childhood abuse and inflammatory markers in adulthood and the extent to which the effects of childhood abuse on inflammatory markers vary over the life course. Moreover, this study evaluates the extent to which these associations are mediated by four plausible pathways: sleep problems, body mass index (BMI), perceived stress, and family social ties. Data come from a biomarker study of the National Survey of Midlife Development in the United States (MIDUS, n = 1,255). I use three inflammatory biomarkers: interleukin (IL)-6, C-reactive protein (CRP), and fibrinogen. To test the selective mortality hypothesis, I consider both all-cause mortality and attrition between the surveys of MIDUS I and MIDUS II. Using latent class analysis, I identify five distinct profiles of childhood abuse. To assess the age-related patterns of inflammatory markers associated with the experience of childhood abuse, the five abuse groups are categorized into two groups: no abuse and abuse. I find significant main effects and age-by-abuse interaction effects on inflammatory markers. In the younger age groups (ages 34-44 and 45-54), victims of childhood abuse have elevated markers of inflammation for all three biomarkers, compared to non-victims. Yet, there are no significant effects of childhood abuse on elevated markers of inflammation in the older age groups (ages 55-

64 and 65-84). Victims of childhood abuse, compared to non-victims, have greater mortality and attrition rates between MIDUS I and MIDUS II, suggesting selective mortality might contribute to a reduced gap in the markers of inflammation between the victims and non-victims in the older age groups. High BMI, poor sleep quality, and weak family social ties partially explain why the experience of childhood abuse increases the levels of inflammatory markers. High BMI, in particular, is the most significant mediator for all the inflammatory biomarkers. My findings highlight the importance of life course stages in understanding the effects of childhood abuse and its adverse health consequences. Targeted interventions to prevent the consequences of childhood abuse need to be started at an early age in order to help reduce the risk that individuals will develop chronic diseases through elevated markers of inflammation in adulthood.

Keywords

stress; childhood abuse; inflammation; age; sleep problems; body mass index; social ties; perceived stress

Introduction

A life course perspective on health emphasizes the importance of early life experiences in the development of chronic diseases in adulthood (Kuh et al. 2003). Numerous studies have indicated that traumatic stress in early life, such as childhood abuse, increases the risk of developing various chronic diseases. Both clinic- and population-based studies have reported that victims of childhood abuse are particularly susceptible to developing disorders, such as allergies and asthma (Felitti et al. 1998; Lanier et al. 2010), autoimmune disorders (Dube et al. 2009), and osteoarthritis (Fuller-Thomson et al. 2009). Stress-induced immune dysfunction and unregulated inflammation may explain the elevated risk of developing these types of diseases among victims of childhood abuse. Chronic stress and/or traumatic stress interfere with the activation of the parts of the brain which are associated with the secretion of the stress hormone cortisol, one of the most important anti-inflammatory hormones. Abnormal cortisol levels, due to chronic and/or traumatic stress, can lead to a high concentration of inflammation biomarkers, such as interleukin (IL)-6 and C-reactive protein (CRP) in the body (Kiecolt-Glaser et al. 2003). Elevated inflammation levels play important roles in developing various chronic diseases (e.g., cancer and cardiovascular diseases) and in increasing the mortality rate (Danesh et al. 1998; Harris et al. 1999).

An emerging body of research has demonstrated the associations between early life adversities (e.g., childhood abuse and living with a substance abuser) and elevated markers of inflammation in both young adulthood (Danese et al. 2007; Taylor et al. 2006) and midlife (Slopen et al. 2010). The associations are consistently significant even after controlling for potential confounders and mediators (e.g., demographics, socioeconomic status [SES]). While timely public interventions play a major role in reducing health inequalities and may decrease the overall cost of care, few researchers have studied whether the effect of childhood abuse on physiological dysregulation (e.g., inflammation) varies over the life course.

Selective mortality and "age-as-leveler" theories suggest that differences in health status by SES are the largest at middle age and converge in later years, perhaps due to premature death

among individuals of lower SES or due to biological fragility among old people regardless of

their SES (House et al. 2005). Similarly, disparities in levels of inflammatory markers between

victims and non-victims of childhood abuse might be narrower with age. Victims of childhood

abuse, compared to non-victims, are less likely to achieve higher SES (Currie and Widom 2010),

and they are more likely to experience subsequent negative life events (e.g., incarceration)

(Widom and Maxfield 2001). Given these cumulative life burdens and physiological loads,

victims of childhood abuse, compared to non-victims, might have elevated markers of

inflammation at earlier ages and may die younger. Accordingly, disproportionate attrition rates

due to illness and premature death might eventually reduce the gap in levels of inflammatory

markers between victims and non-victims of childhood abuse in old age.

In addition, psychological and behavioral factors might contribute to understanding the

association between childhood abuse and elevated markers of inflammation. The literature

documents that unhealthy conditions, including poor sleep quality (Friedman et al. 2005a),

elevated perceived stress (McDade et al. 2006), high body weight (Visser et al. 1999), and small

social networks (Loucks et al. 2006), are particularly associated with a high concentration of

inflammatory markers in the body (Kiecolt-Glaser et al. 2003). Victims of childhood abuse are

more likely to experience these unhealthy conditions (Bentley and Widom 2009; Danese et al.

2009; Gotlib and Wheaton 1997; Greenfield et al. 2011). Although previous research on

childhood abuse and inflammation (Danese et al. 2009; Slopen et al. 2010) has included some of

these factors as either mediators or controls, to my knowledge no research has studied the extent

to which sleep quality and the quality of adult social relationships are potential mediators that link

childhood abuse to levels of inflammatory markers. Additionally, most prior studies that link

childhood abuse to elevated markers of inflammation are limited to samples consisting of young

adults. Further research is needed to understand the diverse mechanisms in older adults.

Using data from the National Survey of Midlife Development in the U.S. (MIDUS), my

study aims to address three issues which have not been fully investigated in prior studies. First, I

investigate the effects of childhood abuse on levels of inflammatory markers in midlife and beyond. I also test whether the effects of childhood abuse decrease in magnitude, or even disappear, with an increase in age. Finally, I examine multiple pathways which might connect childhood abuse to levels of inflammatory markers in adulthood.

Background

According to a life course perspective on chronic disease, childhood experiences play an important role in the development of adult diseases (Kuh et al. 2003). Research has demonstrated that individuals who experience adversities in childhood (e.g., poverty, family violence) have an increased risk of developing various chronic diseases, such as psychological disorders, cardiovascular diseases, diabetes, and cancer. In particular, victims of childhood abuse, compared to non-victims, have an elevated risk of developing such chronic diseases even after controlling for poor family environments in childhood (Springer 2009). Both clinic- and population- based studies have indicated that victims of childhood abuse are especially vulnerable to certain types of diseases over the life course, such as asthma in childhood (Lanier et al. 2010), autoimmune diseases in adulthood (Dube et al. 2009), and multiple sclerosis in adulthood (Spitzer et al. 2012). These types of diseases are directly or indirectly related to altered immune function, such as abnormally enhanced or prolonged inflammation, in response to stressful conditions. This evidence raises a question: how does the experience of childhood abuse influence the immune system and ultimately increase susceptibility to such diseases?

Stress and Inflammation

According to theories related to stress and immunity, psychological stress and negative emotions can alter activities in important brain structures, including the hippocampus and amygdala; the hippocampus is related to the intake and interpretation of sensory stimuli while the amygdala is associated with the generation of emotions based on appraisals (Lovallo 2005). Through these mechanisms, stress stimulates two brain systems, the hypothalamic-pituitary-

adrenal (HPA) axis and sympathetic-adrenal-medullary (SAM) axis, which release diverse stress hormones, for example, adrenocorticotrophine (ACTH) and cortisol (Lovallo 2005). These hormones ultimately influence immune function in two different ways: 1) by directly interacting with immune cells which have stress hormone receptors and 2) by indirectly inducing the production of cytokines (Glaser and Kiecolt-Glaser 2005). Thus, the regulation of stress hormones plays a role in controlling immune functions, including the inflammatory process.

Generally, inflammation is a series of processes that fight against the invasion of viruses or bacteria, detecting invading pathogens, accumulating white blood cells at the site of infection, eliminating the pathogens, and repairing tissue damage. The entire process is orchestrated by inflammatory cytokines (e.g., interluekin-1ß, IL-6, tumor necrosis factor-α), which are molecules secreted by white blood cells. However, without regulation, healthy tissues are damaged by the secretion of massive amounts of inflammatory cytokines; extreme levels of cytokines can even be lethal (e.g., toxic shock syndrome) (Lovallo 2005).

Animal studies show that secretion of the stress hormone cortisol is associated with inflammatory response. After a prolonged period of hyperactivity of the HPA axis, due to chronic or extreme stress, the HPA axis becomes prone to "down-regulate" in response to stress (Gómez et al. 1996), and this hypo-activity of the HPA axis results in the secretion of lower levels of stress hormones (Moncek et al. 2001), which eventually leads to the development of severe chronic inflammation of the joints, such as arthritis (Sternberg et al. 1989). These findings suggest that unregulated inflammation occurs under extreme stress through the dysregulation of stress hormones.

Moreover, research documents significant associations between life stress and altered immune function in humans. The experience of chronic stress and/or negative life events is significantly associated with elevated levels of inflammatory cytokines. For example, older adults who take care of spouses with dementia display increased levels of interleukin (IL)-6, one of the well-known cytokines that increases inflammatory processes (Kiecolt-Glaser et al. 2003).

Another study shows that parents who have been caring for children with cancer display a diminished suppression of IL-6 in a glucocorticoid sensitivity test, which suggests that chronic stress might impair some immune functions through cortisol dysregulation (Miller et al. 2002). Childhood abuse has also been implicated in these associations.

The Associations between Childhood Abuse and Elevated Markers of Inflammation

Studies show that there are significant associations between early life adversities and elevated levels of single and/or multiple inflammatory markers, including IL-6, CRP, and fibrinogen in adulthood. For example, a prospective longitudinal study shows that childhood abuse and neglect are significantly associated with increased levels of inflammation markers (CRP and fibrinogen) in young adulthood (age 32 years); the association between childhood abuse and high sensitive CRP levels remains significant, even after accounting for potential confounders, including early life risks (low birth weight and childhood SES), perceived adult stress, adult health, and health behaviors (Danese et al. 2007). A study, based on a retrospective report of early life adversities, shows that low SES and harsh family environments in childhood (e.g., living with a substance abuser and/or experiencing physical and/or emotional abuse) are significantly related to elevated CRP in young adulthood (average age 40) through pathways involving psychological problems and a high body mass index (BMI) (Taylor et al. 2006).

Another retrospective study indicates that experiencing more stressors throughout childhood and adolescence (e.g., abuse, poverty, dropping out of school, parental alcoholism) is associated with higher levels of multiple inflammatory markers (e.g., IL-6, CRP, fibrinogen) in midlife (average age 56) for African Americans but not for Whites. The significant effects of early life adversities on the elevated markers of inflammation among African Americans either is reduced or disappears after accounting for several factors encountered throughout adulthood, including stressful life events, health conditions, and risky health behaviors (Slopen et al. 2010), suggesting that later negative life events and unhealthy habits in adulthood contribute to part of the association between childhood abuse and levels of inflammatory markers. These three studies

show important evidence of the associations between childhood abuse and inflammation, yet,

Danese et al. (2007) and Taylor et al. (2006) are limited to a sample which includes only young

adults and Slopen et al. (2010) and Taylor et al. (2006) use multiple generic adversities in

childhood as a predictor. It is important to replicate these studies using a sample of individuals

with different ages and to disentangle the effects of childhood abuse on inflammation from the

effect of other childhood adversities (e.g., poverty). Thus, the first hypothesis I test is:

> **Hypothesis 1**: The experience of childhood abuse will be associated with
>
> elevated levels of inflammatory markers among adults (ages 34-84), even after
>
> controlling for adverse childhood environments.

Do the Effects of Childhood Abuse on Elevated Markers of Inflammation Vary over the

Life Course?

Little research has paid attention to whether the effects of childhood abuse on elevated

markers of inflammation are consistent across different age groups. Research indicates that

elevated levels of inflammation predict an increased risk of morbidity (Danesh et al. 1998) and

mortality (Alley et al. 2007). Therefore, because individuals who were abused during childhood

have elevated markers of inflammation, they are at increased risk of death, which might

eventually lead to decreasing age variations in the gap of levels of inflammatory markers between

victims and non-victims of childhood abuse across the life course. Selective mortality theory

helps us to understand the potential age patterns of the effects of childhood abuse on levels of

inflammatory markers. According to this hypothesis, differences in health status by SES are the

largest at around middle age and then are narrowed in old age or disappear in later old age

(Crimmins et al. 2009; House et al. 2005). In other words, health and mortality differentials at

earlier ages lead to a nonrandom selection by SES, which eventually results in a decrease in

health inequality in later life. Thus, some of the victims of childhood abuse who were exposed to

several negative events and who have low SES and weak social ties might have a greater risk of

premature death, which might eventually reduce the differences in inflammation levels between victims and non-victims of childhood abuse in old age. Thus, I would suggest a second two-fold hypothesis:

Hypothesis 2a: Disparities in levels of inflammatory marker between victims and non-victims of childhood abuse will narrow with increasing age.

Hypothesis 2b: Victims of childhood abuse, compared to non-victims, will have greater attrition rates due to death, which may explain why the gap in levels of inflammatory markers between victims and non-victims diminishes in old age.

Psychosocial and Behavioral Pathways Linking Childhood Abuse and Elevated Markers of Inflammation

Numerous studies have documented that victims of childhood abuse have a greater chance of having various unhealthy conditions and engaging in unhealthy behaviors, which are known risk factors for elevated markers of inflammation. Based on the literature, I consider four plausible psychosocial and behavioral pathways linking childhood abuse to elevated markers of inflammation: sleep quality, perceived stress, body mass index, and family social ties.

First, *poor sleep quality*, which is common among victims of childhood abuse (Greenfield et al. 2011), increases levels of inflammatory markers for both healthy and unhealthy individuals over different ages. For instance, people with obstructive sleep apnea, a sleep disorder characterized by abnormal pauses in breathing or instances of abnormally low breathing during sleep, tend to have elevated CRP levels (Shamsuzzaman et al. 2002). In healthy young women, self-reported poor sleep quality is associated with increased levels of CRP, but there is no significant association between poor sleep quality and IL-6 (Okuna et al. 2009). For women aged 61-90, poor sleep quality is significantly associated with elevated levels of IL-6 (Friedman et al. 2005a). Accordingly, individuals with a history of childhood abuse might have elevated markers of inflammation due to trouble sleeping, yet to my knowledge no prior study investigates the

extent to which sleep problems mediate the association. Following from these prior findings, I propose a first hypothesis related to these plausible pathways:

> **Hypothesis 3a**: Poor sleep quality will mediate the positive association between childhood abuse and elevated levels of inflammatory markers.

Second, high levels of *perceived stress* might link the experience of childhood abuse to elevated levels of inflammatory markers. Research indicates that long-term caregivers (ages 55 to 89), who take care of spouses who have dementia, report significantly more perceived stress and loneliness than non-caregivers, and they have elevated levels of IL-6 compared to their counterparts (Kiecolt-Glaser et al. 2003). Another study indicates that more perceived stress is significantly related to elevated levels of CRP in middle-aged and older adults (ages 52 to 72), even after accounting for demographic characteristics and health behaviors (McDade et al. 2006).

Individuals who were abused during childhood appear to experience high levels of stress in adulthood (Hyman et al. 2007). Research indicates that individuals who are exposed to adverse circumstances in early life have a greater risk of being exposed to additional adversities in later life, namely stress proliferation (Pearlin et al. 2005), which might increase sensitivity to stressful situations and cause elevated markers of inflammation. Danese et al. (2007) find that the experience of childhood abuse predicts both increased levels of CRP and high levels of perceived stress for young adults (average age of 32). Yet, perceived stress does not operate as a significant mediator in the association between childhood abuse and increased levels of CRP for these young adults when demographic characteristics (e.g., SES, gender) and medications are accounted for (Danese et al. 2007). Since negative life events and stress accumulate with age, it is necessary to replicate the Danese et al. (2007) study in older populations. Thus, I hypothesize a second mediating association:

Hypothesis 3b: High perceived stress will mediate the positive association between childhood abuse and elevated levels of inflammatory markers.

Third, *BMI* is significantly associated with elevated markers of inflammation. Research finds that obese people are more likely to be in a state of chronic inflammation, as indicated by elevated inflammatory markers, such as IL-6 and CRP (Dandona et al. 2004). For example, young adults (age 17-39) who are overweight or obese are more likely to have elevated CRP levels than those who have healthier body weights (Visser et al. 1999). A prior study finds that BMI mediates the association between early life adversity (e.g., childhood abuse) and elevated markers of inflammation (e.g., IL-6) for African Americans in midlife (Slopen et al. 2010). Another study finds that early life adversity (e.g., physical and emotional abuse) appears to be significantly associated with elevated CRP through high BMI (Taylor et al. 2006). These studies show that experiencing multiple early life stressors is significantly associated with elevated markers of inflammation through high BMI, yet it is hard to specify which form(s) of early stressors play(s) a significant role in increasing inflammation.

Research shows that victims of childhood abuse have an increased risk of being overweight and obese after controlling for early life environments, negative coping skills, and unhealthy habits (Bentley and Widom 2009). Thus, individuals who experienced childhood abuse, regardless of other early life adversities (e.g., poverty), might have elevated markers of inflammation due to uncontrolled body weight. Accordingly, I hypothesize a third mediating association:

Hypothesis 3c: High BMI will mediate the positive association between childhood abuse and elevated levels of inflammatory markers.

Finally, the stress-buffering hypothesis (Cohen and Wills 1985) indicates that strong or high-quality social ties operate as protectors from the potential pathogenic effects of stressful life

events. That is, strong social ties and support mitigate the effects of stressful events on perceived stress and helps individuals utilize positive coping skills and health-promoting behaviors in order to relieve stress (Cohen 2004). Studies find that poor emotional relationships and social isolation are associated with elevated markers of inflammation. For example, for women in midlife and old age, a high degree of social engagement buffers the effect of poor sleep quality on elevated markers of inflammation, decreasing levels of IL-6 (Friedman et al. 2005a). Another study shows that for both men and women in midlife (average age 62), the size of their social network, measured by the Berkman–Syme Social Network Index (Berkman and Syme 1979), is inversely associated with levels of inflammatory markers (e.g., IL-6); the association remain significant for men but not for women even after adjusting for potential confounders (e.g., BMI and SES) (Loucks et al. 2006). Individuals with a history of childhood abuse, in general, may have insufficient social resources (e.g., poor marital quality and social isolation) (Gotlib and Wheaton 1997) that might further increase their vulnerability to stressful situations. In contrast, sufficient social ties and the utilization of social resources may operate as countervailing factors protecting against life's stressors even for victims of childhood abuse and may help them avoid having elevated markers of inflammation. Based on extensive evidence in the literature, I propose a final hypothesis for the mediating associations:

> **Hypothesis 3d**: Strong social ties will attenuate the positive association between childhood abuse and levels of inflammatory markers.

Data and Methods

Sample

The sample for my study (n=1,255) comes from two subsamples of the Midlife Development in the United States (MIDUS) biomarker study: one from the respondents who participated in both the MIDUS I (1995-1996) and MIDUS II (2004-2005) surveys, and the other from a supplementary sample of African Americans from Milwaukee, Wisconsin (2004-2005),

called the Milwaukee sample. The data for the biomarker study came from a two-day data-collection protocol at the General Clinical Research Center (GCRC). The data were collected between 2004 and 2009. Participants stayed overnight at the GCRC and completed the protocol with a clinician. This special module includes diverse biomarkers and a detailed medical history as well as more comprehensive questions regarding childhood abuse than those in MIDUS I. The data collection for MIDUS was approved by the Health Sciences Institutional Review Board at the University of Wisconsin-Madison.

MIDUS is a national study of health and aging among U.S. residents, aged 25 to 74 (b. 1920-1970), who were first interviewed between 1995 and 1996 (n = 7,108). The baseline study included a national sample, which was obtained through random digit dialing (RDD), and consists of respondents, siblings of many respondents (13% of the MIDUS I sample), and a national sample of twins (24% of the MIDUS I sample) of the same age range as the national RDD sample. Respondents were limited to English speaking, non-institutionalized adults. A longitudinal follow-up of the MIDUS sample was conducted 10 years after the baseline assessment (2004-2005). At that point, a supplemental sample of 592 African Americans from Milwaukee, Wisconsin was recruited in order to investigate health in a highly segregated U.S. city. MIDUS II assessed a wide array of psychological constructs and demographic characteristics as well as extensive health measures. Based on the primary survey, four additional projects (Daily Diary Study, Cognitive Function, Bioindicators, and Neuroscience) were conducted to explore the biopsychosocial pathways to various health outcomes (Love et al. 2010).

Of those who initially responded to the questions in the MIDUS I, 70% were interviewed in the MIDUS II and 21% of the MIDUS II sample (n =1,054) and 39 % of Milwaukee sample (n = 201) attended the clinical examination, resulting in a total of 1,255 respondents. Compared to the respondents in the primary national sample (MIDUS I), those in this subsample had higher levels of education and personal income, visited doctors more frequently, and maintained an overall healthier life style (e.g. non-smokers). They were, however, similar to the other

respondents in terms of demographic (e.g., age, gender, and marital status) and health

characteristics (for a more detailed description of the study, consult Love et al. 2010).

Measures

  Dependent Variables. On the basis of prior research on inflammatory markers, I select

three of the commonly used biomarkers for inflammation (IL-6, CRP, and fibrinogen) and the

summary of these markers, called the inflammatory index. CRP and fibrinogen are molecules

produced in the liver in response to IL-6 (Friedman and Herd 2010). Like IL-6, high levels of

CRP and fibrinogen are clinical signals of elevated risk of inflammation in the body (Danesh et

al. 1998). Fasting serum samples are assayed for CRP, IL-6, and fibrinogen, based on the

manufacturer guidelines (Dade Behring Inc., Deerfield, IL for CRP and fibrinogen; R&D

Systems, Minneapolis, MN for IL-6). Immunonephelometric assay is performed for the citrated

plasma CRP and fibrinogen assay and enzyme-linked immunosoben assay is performed for the

IL-6 assay. For all three inflammation markers, the laboratory intra- and inter-assay coefficients

of variance are in acceptable ranges ($< .13\%$) (Ryff et al. 2010). IL-6 (*mean* = 3.04; SD = 3.04;

skewness = 3.32) and CRP (*mean* = 3.02; SD = 4,02; *skewness* = 5.78) are log-transformed to

improve the normality of the distribution, which is consistent with prior studies (Danese et al.

2007; Slopen et al. 2010). The inflammatory index is a summary of the high risk cut offs of the

three inflammatory markers and ranges from 0 to 3: CRP (≥ 3.0 mg/L), fibrinogen (≥ 341 mg/dL

for men and ≥ 411 mg/dL for women) and the top quartile of the IL-6 level distribution ($>$

3.47pg/dL). Tetrachoric correlations between these three markers range from .49 to .57. Research

indicates that top 25% of IL-6 and high CRP (≥ 3.0 mg/L) are associated with mortality in the

elderly (age 65+) (Harris et al. 1999) and coronary health disease for all adults (Danesh et al.

1998).

  Independent Variable. *Childhood abuse history.* Childhood abuse is used as a key

indicator of traumatic stress during childhood. The Childhood Trauma Questionnaire (CTQ;

Bernstein and Fink 1998) is used to evaluate the severity of physical, emotional, and sexual abuse

up to the age of 16. The CTQ is a well-validated questionnaire that contains 25 items divided

among five subscales to assess the three different types of abuse (physical, emotional, and sexual)

and two different types of neglect (physical and emotional). It also includes a three-item scale for

minimization and denial to identify respondents who are more likely to underreport negative

events in childhood (e.g., "I had the best family in the world"). Respondents answered questions

about childhood abuse/neglect and minimization/denial, which were measured on a scale ranging

from 1 = "never true" to 5 = "very often true". Based on the 15 CTQ items, including the three

types of abuse, and on the composite score from the three minimization/denial items, I conduct

latent class analysis (LCA) and create five classes of childhood abuse history (for details about

latent classes of childhood abuse, see Chapters 2 and 3). Since the sample size is too small to test

the age-by-abuse interaction effects for all the LCA classes, I create a dichotomous measure of

childhood abuse: *no abuse* (65%) vs. *abuse* (35%) including the four abuse classes from the LCA

(see note 2).

    Psychosocial and Behavioral Mediators. *Sleep Quality.* The Pittsburgh Sleep Quality

Inventory (Buysse et al. 1989), which is one of the most widely used subjective sleep quality

scales of measurement based on respondents' self-reports, is used to evaluate sleep difficulties.

This includes seven sleep components: 1) subjective sleep quality, 2) sleep latency, 3) sleep

duration, 4) habitual sleep efficiency, 5) sleep disturbance, 6) use of sleep medications, and 7)

daytime dysfunction. The response to items for each component ranges from 0 to 3, with the

higher scores indicating poorer subjective sleep quality. I use a summary index of the seven sleep

components as a measure of sleep quality, ranging from 0 to 21, which is consistent with the

measures used in prior studies (Friedman et al. 2005a; Okuna et al. 2009).

    Body Mass Index (BMI) is based on the data (body weight (kg)/ [height (m)]^2) measured

by the GCRC staff. BMI is used as a continuous variable (*Mean* = 29.77; SD = 6.62), which is

consistent with prior studies (Slopen et al. 2010; Taylor et al. 2006). The 10-item *perceived stress*

scale (Cohen et al. 1983) assesses the degree to which participants were consciously aware that

their daily lives were unpredictable, uncontrollable, and overloaded with life stress during the week prior to the interview. Participants rated each item from never (=1) to very often (=5). A composite scale score of the 10 items ranges from 10 to 50, a higher score indicating higher levels of perceived stress (*Mean* = 22.24; SD = 6.36; alpha =.86). *Family social ties,* which does not include spouse/partner, is a 6-item scale combining the two items about "support given to family" (family rely on respondents for help with serious problems and family discuss their worries with respondents), and four items about "strain given to family" (making too many demands on family, criticizing family members, letting family down when they are counting on respondents, and getting on family's nerves). The 6 items are coded consistently, with a high score signifying high levels of "family affectual solidarity" (1 = not at all through 4 = a lot). The scale of family social ties is constructed by calculating the mean of the values of the 6 items ranging from 1 to 4 (*Mean* = 3.43; SD = .37). I did not include strain or support given to a spouse/partner as a part of family social ties since 35% of respondents did not have a spouse/partner (31% of non-victims and 43% of victims). Prior studies indicate that strong social ties are associated with health-promoting behaviors and positive health outcomes (Grzywacz and Marks 1999; Kawachi and Berkman 2001).

Control Variables. To thoroughly test and describe age variation in the effect of childhood abuse on inflammation, I use two different measures of the ages of the respondents at the time of MIDUS II (34-84 years old): a linear covariate for testing the age-by-abuse interaction effect and a categorical variable (ages 34-44, 45-54, 55-64, and 65-84) for better visualizing the age-by-abuse interaction effect. The first age category (ages 34-44) is made up in order to compare findings in the current study and those in prior studies on early life adversities in young adulthood (Danese et al. 2009; Taylor et al. 2006). The second and third categories (ages 45-54 and ages 55-64) are selected based on a prior study based on the selective mortality hypothesis (Robert et al. 2009). Given a small sample size for older people (age 65+), particularly for victims

of childhood abuse (14% of the sample), the fourth category of age consists of all respondents who are age of 65 or older.

In order to disentangle the effects of childhood abuse on inflammation from other early life adversities and potential confounders, this study includes five sets of covariates: demographic characteristics, such as SES and marital status (Friedman and Herd 2010; Loucks et al. 2006; O'Connor et al. 2009), childhood environment (Slopen et al. 2010), chronic diseases (Alley et al. 2007), as well as medications, which are significantly related to inflammation markers. Demographic variables include gender (1 = female), race/ethnicity (white/non-white) and current marital status (married/cohabiting = 1 vs. separated, divorced, widowed, or never married = 0) at the time of the Bioindicators assessment. SES is assessed by the participants' educational attainment (less than high school [reference], high school, college, more than maters' degree).

For the childhood contexts, I use the highest level of parental (mother's or father's) education (less than high school [reference], high school, more than high school), whether the respondents lived with both their biological parents until the age of 16 (yes/no), and whether the family was on welfare or Aid to Dependent Children (ADC) during childhood (yes/no).

History of chronic disease indicates whether the respondents have experienced a stroke or have either diabetes or cancer (yes/no). I include the use of four types of medication: blood pressure medication (yes/no), cholesterol-lowering medication (yes/no), steroids (yes/no), and antidepressants (yes/no), as inventoried by the GCRC staff. I adjust for use of these medications based on research showing the effect of these medications on circulation of inflammatory markers

Attrition. To assess the selective mortality hypothesis, I make two dichotomous indicators of attrition rates: all causes of attrition (yes/no) and all causes of mortality (yes/no), to examine whether the abused survivors were more likely than the non-abused respondents to fail to participate in the 2004 survey (MIDUS II) (see note 1). These two indicators are consistent with a prior study regarding non-random attrition for victims of childhood abuse (Springer 2009).

I use self-reported mental health, physical health, demographics, and childhood contexts as controls for the attrition test.

Analytic Strategy

After the LCA of childhood abuse, analyses are carried out in four stages: 1) bivariate analyses for characteristics of victims and non-victims of childhood abuse; 2) multivariate analyses in order to test the age-by-abuse interaction effects; 3) mediation modeling to identify potential mediators; and 4) supplementary analyses to test the selective mortality hypothesis.

In order to carry out subsequent analyses, in the first stage, I conduct bivariate analyses to evaluate whether the childhood abuse groups differ in potential mediators and controls. In the second stage, to examine the age variations in the associations between childhood abuse and inflammation outcomes, I first test the main effects of childhood abuse on each inflammation marker after adjusting for all controls. Second, I include the interaction term between childhood abuse and the linear measure of age. To understand the pattern of the effects of childhood abuse on inflammation by age, I graph the mean values of each individual inflammation maker within the abuse groups and the four age groups (ages 34-44, 45-54, 55-64, and 65-84) with a 95% confidence interval (CI). Multivariate ordinary least squares (OLS) and zero-inflated Poisson regression are used to determine the associations between childhood abuse and linear inflammatory markers (logged IL-6, logged CRP, and fibrinogen) and a count measure of the inflammatory index, respectively.

In the third stage, I test the effects of potential mediators (Baron and Kenny 1986), examining the extent to which each mediator significantly accounts for the association between childhood abuse and risk of elevated inflammation levels. The four sets of mediators enter into the model, separately. To check whether the mediators carry the effects of childhood abuse to elevated markers of inflammation, I use a Sobel test (Sobel 1982). Finally, in case there are significant age-by-abuse interaction effects on inflammatory markers, I conduct a supplementary analysis for a selective mortality hypothesis to investigate whether abused respondents were more

likely than non-abused ones to fail to participate in the 2004 survey (MIDUS II) and whether the higher attrition rates of abused individuals are due to mortality.

The percentage of missing data is less than 13 percent when I apply listwise deletion. I impute the missing data under the missing-at-random (MAR) assumption (Allison 2001) in order to alleviate the potential statistical power issues in subsequent analyses. All variables, except the dependent variables and a mediator (social support from family, missing n = 6), are included in the imputation procedure. The analyses are carried out using Mplus 6.0 (Muthén and Muthén 2008; Muthén and Muthén 2010) and STATA 11.0 (STATA Corp, 2010). To correct intra-class correlation due to some respondents being from the same family (e.g., twins or siblings, 12.61% in the biomarker study), I apply robust standard error estimation.

Results

Characteristics of Abuse and No Abuse Respondents

Table 3-1 summarizes the results of the bivariate analyses for the characteristics of the abuse group (35% of the respondents) and no-abuse group (65% of the respondents). Individuals with a history of childhood abuse, compared to those who did not experience it, are younger (*Mean* $_{abuse}$ = 51.89 vs. *Mean* $_{no\ abuse}$ = 55.93); there are significant age variations in the two groups. In particular, the individuals who are between 65 and 84 make up 25% of the no-abuse group, while individuals between these ages represent 14% of the abuse group, suggesting there might be a non-random selection bias due to the experience of childhood abuse or cohort differences in reporting rates of childhood abuse. In addition, individuals with a history of childhood abuse tend to be less educated, and they are more likely to be female and non-white. The former are more likely to have grown up in families on welfare and are less likely to have lived with parents until age 16. The mean inflammatory markers for individuals in the abuse group are significantly higher for IL-6 and CRP, and the inflammation index; yet, there is no significant difference between those in the abuse and no-abuse groups for fibrinogen (*p* = .23). Regarding the potential mediators, the individuals in the abuse group have significantly poorer sleep quality, higher

perceived stress, higher BMI, and lower levels of family social ties, compared to those not abused.

[Table 3-1 about here]

Levels of Inflammatory Markers by Abuse and Age

In the baseline models (in Table 3-2), I test the first and second hypotheses regarding whether individuals who experienced childhood abuse have elevated markers of inflammation and whether the effects of childhood abuse on elevated markers of inflammation vary by age after adjusting for all controls. I find that there is not a significant main effect of childhood abuse on inflammatory markers (see model 1 of Table 3-2), however a main effect emerges when the age-by-abuse interaction term is added into the models (see model 2 of Table 3-2), indicating that the effects of childhood abuse on levels of inflammatory makers are not consistent across ages. These life course patterns would have been concealed in a model that failed to evaluate such interaction effects. Figures 3-1 through 3-4 illustrate the means of inflammatory markers by abuse and age groups, after adjusting for all controls. Specifically, Figure 3-1 shows that the experience of childhood abuse is significantly associated with elevated levels of IL-6 for the two younger age groups (ages 34-44 and 45-54) but not for two older age groups (ages 55-64 and 65-84). In the younger age groups, the difference in IL-6 levels between the abuse and no-abuse groups is wider for the 34-44 age group (difference $_{ages\ 34-44}$ = .32) than the 45-54 age group (difference $_{ages\ 45-55}$ = .16). Between the ages of 55-64, there is no significant difference in IL-6 levels between those in the abuse and no-abuse groups. Between the ages of 65-84, the pattern reverses; those in the no-abuse group have greater IL-6 levels than those in the abuse group, although the difference is not significant.

[Figure 3-1 and 3-2 about here]

The results of CRP and fibrinogen shown in Figures 3-2 and 3-3, respectively, show similar patterns to IL-6, except that the fibrinogen levels at ages 65-84 are significantly higher for individuals in the no-abuse group compared to those in the abuse group. Finally, Figure 3-4

shows that the experience of childhood abuse is significantly associated with elevated levels of the inflammatory index for the three youngest age groups (ages 34-44, 45-54, and 55-64), but the association is inversely related for the oldest group (ages 65-84). Overall, the results in Figures 3-1 through 3-4 indicate that a difference in levels of inflammatory markers exists depending on whether the individuals experienced abuse or not; the difference is largest at ages 34-44, smaller at ages 45-54, much smaller at ages 55-64, and disappears between the ages of 65-84.

[Figure 3-3 and 3-4 about here]

Plausible Pathways Linking Childhood Abuse and Elevated Markers of Inflammation

Models 3 to 6 of Table 3-3 show whether the four hypothesized pathways, including poor sleep quality, perceived stress, BMI, and family social ties, explain the association between childhood abuse and levels of inflammatory markers. Model 3 shows that the effects of childhood abuse on all inflammatory outcomes are attenuated after including sleep quality, but the main effects and the interaction effect are still significant. The Sobel tests show that poor sleep quality significantly links childhood abuse to two elevated inflammatory makers: CRP (Sobel test $p < .05$) and the inflammatory index (Sobel test $p < .05$) but not to fibrinogen (Sobel test $p = .49$) and IL-6 (Sobel test $p = .07$). Model 4 includes perceived stress as a mediator; there are no significant main effects of perceived stress on any of the four inflammatory markers. Changes in the estimated main effects and the interaction effect on inflammatory markers are small or change little before and after including perceived stress. These findings indicate that perceived stress does not mediate the associations between childhood abuse and elevated markers of inflammation in adulthood. In Model 5, including BMI as a mediator, all parameter estimates for the main effects of childhood abuse on levels of inflammatory markers are reduced significantly. Results of the Sobel tests indicate that BMI significantly mediates the associations between childhood abuse and all inflammatory markers (all Sobel tests $p < .01$). Model 6 includes social ties as a mediator. After including the mediator, the main effects of childhood abuse on inflammatory markers are reduced substantially but are still significant. Results of the Sobel tests show that family social

ties significantly mediates the association between childhood abuse and elevated IL-6 (Sobel test $p < .05$) but not for fibrinogen levels (Sobel test $p = .06$) and other two inflammatory markers.

Overall, this series of mediation models suggests that the associations between childhood abuse and risk of elevated markers of inflammation partially operate through the effects of childhood abuse on sleep quality, BMI, and/or family social ties. BMI, in particular, is the strongest mediator for all the inflammatory markers.

[Table 3-2 about here]

Supplemental Analyses: Selective Mortality Theory

To expand on the results regarding age variation on the effect of childhood abuse, I examine whether the abused survivors were more likely than the non-abused respondents to fail to participate in the 2004 survey (MIDUS II) The results in Table 3-3 show that the respondents who reported having experienced physical abuse have greater rates of attrition in the 2004 survey (OR = 1.16, 95% CI = 1.01-1.35), compared to the non-abused respondents, after adjusting for controls. In addition, individuals with a history of physical abuse are more likely to leave the 2004 survey due to death (OR = 1.33, 95% CI = 1.03-1.71). There are no age-by-abuse interaction effects on both risk of attrition and risk of death. That is, the attrition rates and death rates are greater for abused individuals than for non-abused respondents, yet the association does not vary significantly by age. These findings indicate selective mortality might contribute to a reduced gap in the levels of inflammatory markers between victims and non-victims in the older age groups.

[Table 3-3 about here]

Discussion

My study demonstrates that the experience of childhood abuse increases levels of inflammatory markers in adulthood; I find that there are substantial age variations in levels of the markers between the abuse and no-abuse groups. In the younger age groups (ages 34-44 and 45-

54), abused individuals, compared to non-abused ones, have elevated levels of IL-6, CRP, and fibrinogen, and they also have a higher inflammatory index, a summary of these three markers. The differences in levels of inflammatory markers between the two groups are larger for ages 34-44 than for ages 45-54. However, the effects of childhood abuse on most measures of inflammatory markers are no longer statistically significant and even reverse in the older age groups (ages 55-64 and 65-84). Overall, my findings are consistent with those in a prior study showing the effects of childhood abuse on elevated markers of inflammation in young adulthood (Danese et al. 2007). While the Danese et al. (2007) study is limited to a sample with a cohort of children born in the 1970s in New Zealand, my study uses a U.S. nationally representative sample including various cohorts of individuals born between 1920 and 1975. My study reveals that the effects of childhood abuse on elevated markers of inflammation are present only for young adults or adults in early midlife.

The difference in levels of inflammatory markers across age groups within the abuse/no-abuse groups supports the selective mortality hypothesis. The patterns of age-by-abuse interactions in levels of inflammatory markers are similar to the findings in age-by-SES interactions in health outcomes in prior studies (Crimmins et al. 2009). Yet, while SES disparities in health outcomes are the largest around middle age, narrow in old age, and disappear in later old age, disparities in levels of inflammatory markers within the abuse/no-abuse groups are the largest in young adulthood, narrow in midlife, and disappear in old age. Given the cumulative life adversities and low SES achievements that the individuals with a history of childhood abuse have experienced (Currie and Widom 2010; Maxfield and Widom 1996), they might suffer cognitive impairment, physical limitations, and chronic diseases at earlier ages, which can eventually lead to higher mortality rates throughout the life course. These factors might be a reason why the difference in levels of inflammatory markers between these two groups does not exist beyond midlife.

Although cross-sectional data show that patterns of levels of inflammatory markers vary across the life course, research has pointed out that cohort effects might confound these differences (House et al. 2005). Because public attention on childhood abuse and neglect has increased and cultural definitions of abuse have changed over recent decades, individuals in older cohorts might not view corporal punishment (e.g., being punished with hard objects or spanking) as abuse, whereas younger cohorts might report it as abuse. On the other hand, older cohorts might consider the experience of childhood abuse as a stigma, so they may be more likely to underreport their experience of childhood abuse. Thus, cohort differences in the definition of childhood abuse might lead to a bias in the findings regarding the age patterns of inflammation between victims and non-victims of childhood abuse. Due to the nature of the data, this study does not separate the age effect from the cohort effect. Future studies need to consider both the cohort and age effects when addressing childhood abuse and health consequences over the life course.

The findings from supplementary analyses somewhat confirm the selective mortality hypothesis. Abused individuals are more likely to fail to participate in the second wave of the MIDUS study, and one reason is due to higher mortality among abused individuals between 1994 and 2004. I assume risk of death might be greater for abused individuals in old adulthood, compared to in young adulthood, and that might be a plausible explanation for why the effects of childhood abuse on markers of inflammation disappear in later midlife and old age. However, I do not find an age-by-abuse interaction effect on either the attrition or death rates, perhaps because I use short-term longitudinal data including diverse cohorts. On the other hand, it is possible that individuals who experience childhood abuse and survive until old age might have biological robustness and/or resilience, which might help them overcome the harm from childhood abuse.

In additional supplementary analyses, interestingly, I find that there is an age-by-abuse interaction effect on family social ties. An increase in family social ties by age is more dramatic

for victims of childhood abuse than non-victims. That is, disparities in social ties between the abuse and no-abuse groups are largest in the 34-44 age group; these disparities are smaller with advancing age (data available upon request). In the 65-84 age group, there is no significant difference in family social ties between victims and non-victims. Given the association between strong family social ties and health-promoting behaviors (Grzywacz and Marks 1999), the fact that victims of childhood abuse do not have higher levels of inflammatory markers than non-victims in old age might be explained by similarities in the degree of family social ties within each group. Future research needs to apply advanced analysis (e.g., a mediated moderation analysis) to thoroughly investigate these associations.

Findings in the mediation analysis indicate that high BMI, poor sleep quality, and weak family social ties partially explain the pathways through which the experience of childhood abuse increases levels of inflammatory markers. Amid the mediators, high BMI plays a major role linking the experience of childhood abuse to elevated markers of inflammation. Since heavy people tend to have sleep apnea, which compromises their sleep quantity and quality (Wolk et al. 2003), BMI may be a more powerful predictor than sleep. There is also a possibility of reverse causality. That is, the experience of childhood abuse may increase levels of inflammatory markers, and elevated markers of inflammation may increase the risk of being obese. Recent research indicates either that there is a positive association between levels of cytokines in early life and the development of obesity and type 2 diabetes, or that there are common factors (e.g., poor diet) which cause both obesity and elevated markers of inflammation (Litonjua and Gold 2008). Therefore, individuals with a history of childhood abuse might have elevated markers of inflammation via either pathway. It is necessary for future research to include more time points to assess the temporal order between potential mediators and outcomes.

There appears to be an independent association between childhood abuse and levels of inflammatory markers even after accounting for various confounders and mediators. For example, all variables, including childhood abuse, explain up to 26% of the variation of CRP levels.

Unobserved and unmeasured factors in this study might potentially explain the rest of the variation. These might include common genetic predictors, maternal nutrition during pregnancy, birth weight, and infant weight gain (Barker et al. 2002). Unhealthy behaviors over the life course, including insufficient exercise, sedentary activity, poor diet, smoking, and alcohol use, might also explain why abused individuals have elevated levels of inflammatory markers. Being exposed to poor physical environments (e.g., crowded or poor housing conditions, and toxic exposures) (Cohen et al. 2010) might also increase the risk of being exposed to pathogens and elevate the markers of inflammation for abused individuals. Additionally, given the strong association between early life and adult victimization (Bensley et al. 2003), elevated markers of inflammation in adulthood might be explained by the experience of abusive relationships in adulthood (e.g., intimate partner violence). Accordingly, future research should consider investigating the extent to which these multiple factors lead to elevated markers of inflammation in victims of abuse.

Limitations and Future Directions

This study has limitations that should be noted. When analyzing the age-by-abuse interaction effects in a relatively small sample, I combine all four abuse groups generated by the LCA into one group, called abuse. Therefore, I do not consider multiple subtypes of abuse or the severity of abuse. In addition, given the relatively small size of the sample, I merge all individuals who are 65 or older into one group (ages 65-84). Future studies need to replicate my study with larger samples, examining various types of childhood abuse across multiple age groups.

Research on the selective mortality hypothesis demonstrates that disparities in health conditions by SES disappear in later old age (House et al. 2005). Individuals who experience abuse as children and survive into later old age might have biological robustness, as well as psychological resiliency; experiencing hardships in early life might help them resist or deal better with later life hardships, such as the death of friends and family members or the need to care for an ill or disabled spouse, which are common difficulties for older people (Glass et al. 1997).

Little research has investigated how long abused individuals will live, and if they are still alive in midlife and beyond, what are the conditions which made them resilient. Some survivors of childhood abuse might develop skills in mobilizing resources, avoiding stressful situations, and adopting positive coping strategies (Walsh et al. 2010) that eventually operate as protective resources against stressors and physiological burdens and increase the individuals' longevity and quality of life. Future studies should explore these factors to better understand the long-term effects of childhood abuse on lifelong health.

Moreover, since the questions about abuse were asked in midlife and required retrospective evaluations of experiences that may have occurred as much as 50 years earlier, a recall bias in reporting childhood abuse must be considered. There might be a possibility that individuals with mood disorders might exaggerate or misrepresent the adversities they experienced during childhood (Widom and Morris 1997). Yet, memories of specific childhood experiences (e.g., positive relationships, negative events, parental discipline) are highly stable (Yancura and Aldwin 2009), and recollections of traumatic events in childhood tend to be fairly accurate (for a review, see Hardt and Rutter 2004). In supplementary analyses, I also find both strong correlation and consistency between reports of physical abuse that were measured at MIDUS I and MIDUS II, with a 10-year gap. In addition, I find no interaction effect of depression diagnosis (in MIDUS II) in the association between reports of physical abuse, possibly indicating that depression does not significantly affect the repeated reports of physical abuse over the 10-year span. Given the use of slightly different measures at the two periods, the measures of self-reported childhood abuse in this study appear quite reliable. In addition, research on stressful events, subjective responses to these events, and the various strategies employed to cope with them has pointed out the importance of considering an individual's subjective perceptions of stressors (Lazarus and Folkman 1984). That is, the way that victims of childhood abuse assess the adversity of early life events might explain whether they adopt negative or positive coping strategies and their concomitant health consequences.

       Despite these limitations, there is much to be learned from this study. Overall, my findings highlight the importance of life course stages in understanding the effects of childhood abuse and its adverse health consequences. In order to help reduce the risk of developing chronic diseases through elevated markers of inflammation in adulthood, targeted interventions to prevent the consequences of childhood abuse (e.g., developing both positive emotional resources and close social ties and controlling body mass index) need to be started at an early age. Furthermore, understanding the complex mechanisms (e.g., the biological, cognitive, emotional, social and behavioral pathways) linking early life adversities to later health outcomes can shed light on how to improve social services and public health interventions for those who have experienced such adversities during childhood.

Notes

1. For the supplementary analyses of attrition rates, I use severe physical abuse measured in MIDUS I. Severe physical abuse consists of five items from Conflict Tactics Inventory (CTI): 1) kicked, bit, or hit you with a fist; 2) hit or tried to hit you with something; 3) beat you up; 4) choked you; and 5) burned or scalded you. Severe physical abuse is coded as a dichotomous variable, 1 indicating that individuals reported "often" or "sometimes" to any of the five CTI items and 0 indicating the others ("rarely" and "never"). Cohen's kappa between severe physical abuse (MIDUS I) and physical abuse (MIDUS II) is .84.5%, indicating a very good agreement (> .81%) and Tetrachoric correlation is .76.

2. Most victims of childhood abuse experienced multiple forms of abuse with different degree, yet most previous studies have been limited to a measure representing a single type of childhood abuse (e.g., emotional, physical, or sexual abuse). Consistent with Chapter 2 and Chapter 3, I conduct latent class analysis and create and five distinct groups of childhood abuse. Due to the statistical power issue in analyzing age-by-abuse interaction terms, I categorize these five groups into two general groups: *abuse* vs. *no abuse*, including four abused groups. For the sensitivity test, I generate a dichotomous measure of childhood abuse, called *anyabuse* (yes = 1 / no = 0): 1 including respondents who answered "sometimes, often, or, very often true" to any of the 15 CTQ items and 0 including respondents who answered "rarely or never true" to all of the 15 CTQ items. Any abuse consists of 53% respondents who reported any type of childhood abuse. I use a dichotomous measure generated by LCA analysis since *anyabuse* (53%) seems to overestimate the prevalence of childhood abuse in the population and 100% of the individuals who are categorized *abuse* also belong to *anyabuse*.

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Table 3-1 Bivariate Analysis for Abuse and No Abuse Respondents

	Abuse (n = 437) Mean (SD)	No Abuse (n = 818) Mean (SD)	Total (n = 1,255) Mean (SD)	χ^2 (df) or t-test (df)
Inflammatory markers				
IL-6 (mg/L)	3.26 (3.25)	2.93 (2.93)	3.04 (3.04)	-1.82 (1241)
CRP (pg/dL)	3.34 (4.88)	2.86 (4.71)	3.02 (4.78)	-1.68 (1233)
FGN (mg/dL)	353.09 (84.43)	346.72 (89.57)	348.92 (87.85)	-1.21(1233)
Inflammatory index (0-3)	.90 (1.01)	.75 (.97)	.80 (.99)	-2.41 (1232)*
Potential mediators				
Poor sleep quality (0-21)	7.41 (3.94)	5.63 (3.36)	6.25 (3.67)	-10.31(1253)***
Perceived Stress Scale (10-50)	24.68 (0.34)	20.94 (0.19)	22.24 (0.18)	-3.80 (1252)***
Body mass index (kg/m^2)	30.73 (7.68)	29.25 (5.93)	29.77 (6.63)	-8.43 (1253)***
Family social ties (1= not at all – 4 = a lot)	3.31(0.40)	3.49 (0.34)	3.43 (0.37)	8.46 (1247)
Covariates				
Age (34-84)	51.89 (10.55)	55.93 (12.05)	54.52 (11.71)	5.91(1253)***
Age groups				
34-44	22	27	23	29.90 (3)***
45-54	26	35	29	
55-64	28	24	27	
65-84	25	14	21	
Female	68	51	57	31.24 (1)***
White	73	81	78	10.27 (1)**
Parental education				
Less than high school	28	24	25	2.57 (2)
High school	34	34	34	
More than high school	38	42	41	
Living with parents until age 16	71	81	77	13.7 (1)***
Family on welfare in childhood	16	6	9	36.9 (1)***
Married/cohabitating	57	69	65	15.5 (1)***
Education				
High school or less	31	26	28	11.6 (3)**
Less than college	33	28	30	
College	16	22	20	
MA or more	19	23	22	
Chronic diseases [a]	24	28	27	2.23 (2)
Medications				
Antihypertension	35	37	37	0.46 (1)
Anticholesterol	24	30	28	5.37 (1)*
Steroids	14	11	12	1.22 (1)

Note: [a] chronic diseases indicate whether the respondents have experienced a stroke or have either type 2 diabetes or cancer.

Table 3-2 Main and Mediation Effects of Childhood Abuse on Inflammatory Markers through Plausible Pathways

	IL-6 (log) n = 1,239	CRP (log) n = 1,231	Fibrinogen n = 1,231	Inflammation Index n = 1,230
Model 1. Baseline Model				
Abuse	.06 (.05)	.05 (.07)	.91 (5.14)	.08 (.07)
Age	.01 (.002)***	-.005 (.003)	.82 (.26)**	.003 (.003)
Model fit	R^2 = .150	R^2 = .103	R^2 = .117	χ^2 (df) = 145 (17)
Model 2. Interaction Model				
Abuse	.49 (.21)*	.92 (.35)**	64.12 (23.78)**	.80 (.35)*
Age	.01 (.002)***	.0003 (.004)	1.19 (.30)***	.008 (.004)*
Abuse × Age	-.008 (.004)*	-.02 (.006)**	-1.19 (.44)**	-.01 (.006)*
Model fit	R^2 = .153	R^2 = .108	R^2 = .122	χ^2 (df) = 146 (18)
Model 2. Poor Sleep				
Abuse	.46 (.21)*	.87 (.35)**	62.92 (23.88)**	.75 (.36)*
Age	.01 (.002)***	.001 (.004)	1.20 (.30)***	.008 (.004)*
Abuse × Age	-.008 (.004)*	-.02 (.006)**	-1.18 (.44)**	-.01 (.006)*
Poor Sleep Quality	.01 (.006)†	.02 (.01)*	.49 (.71)	.02 (.009)*
Model fit	R^2 = .156	R^2 = .113	R^2 = .122	χ^2 (df) = 153 (19)
Model 3. Perceived Stress				
Abuse	.48 (.21)*	.95 (.34)**	64.15 (23.77)**	.79 (.35)*
Age	.10 (.002)***	-.00004 (.004)	1.19 (.30)***	.008 (.004)*
Abuse × Age	-.008 (.004)*	-.02 (.006)**	-1.19 (.44)**	-.01 (.006)*
Perceived Stress	.001 (.003)	-.005 (.006)	-.007 (.38)	.001(.005)
Model fit	R^2 = .153	R^2 = .109	R^2 = .122	χ^2 (df) = 147 (19)
Model 4. BMI				
Abuse	.42 (.21)*	.79 (.31)**	57.52 (22.77)*	.65 (.35)
Age	.01 (.002)***	.005 (.004)	1.42 (.29)***	.01 (.004)**
Abuse × Age	-.008 (.004)*	-.02 (.006)**	-1.14 (.43)**	-.01 (.006)

BMI	.03 (.003)***	.07 (.005)***	3.48 (.43)***	.05 (.004)***
Model fit	$R^2 = .223$	$R^2 = .257$	$R^2 = .182$	χ^2 (df) = 338 (19)
Model 5. Family Social Ties				
Abuse	.43 (.21)*	.88 (.35)*	57.31 (23.87)*	.73 (.35)*
Age	.01 (.002)***	.0002 (.96)	1.18 (.30)***	.008 (.004)
Abuse × Age	-.007 (.004)	-.02 (.006)*	-1.11 (.44)*	-.01 (.006)
Family Social Ties	-.12 (.06)*	-.09 (.09)	-13.50†	-.15 (.09)
Model fit	$R^2 = .156$	$R^2 = .109$	$R^2 = .125$	χ^2 (df) = 147 (19)

Note. All control variables (demographics, childhood environments, chronic diseases, SES, and medications) are adjusted for the models.

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

Table 3-3 Risks of Attrition and Mortality by Abuse and No-abuse Groups between MIDUS I (1994) and MIDUS II (2004)

	Odds of Attrition (n = 5,814)		Odds of Death (n = 5,814)	
	OR	95% CI	OR	95% CI
Severe physical abuse in childhood	1.16*	(1.00-1.33)	1.33*	(1.04-1.71)
Demographics				
Age	.93*	(.87-.98)	2.82***	(2.45-3.26)
Female	.77**	(.68-.88)	.75*	(.60-.93)
White	.45**	(.37-.54)	1.00	(.67-1.51)
Childhood context				
Parental education				
Less than high school (Reference)	1.00		1.00	
High school	.84*	(.72-98)	.94	(.73-1.21)
More than high school	.64*	(.54-.75)	.96	(.73-1.27)
Family on welfare in childhood	1.29*	(1.02-1.63)	1.25	(.83-1.88)
Health status (MIDUS I)				
Physical health	.75***	(.70-.81)	.51	(.45-.57)***
Mental health	1.01	(.94-1.09)	1.21	(1.07-1.38)**
χ^2 (df)	240.55 (9)		528.42 (9)	

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

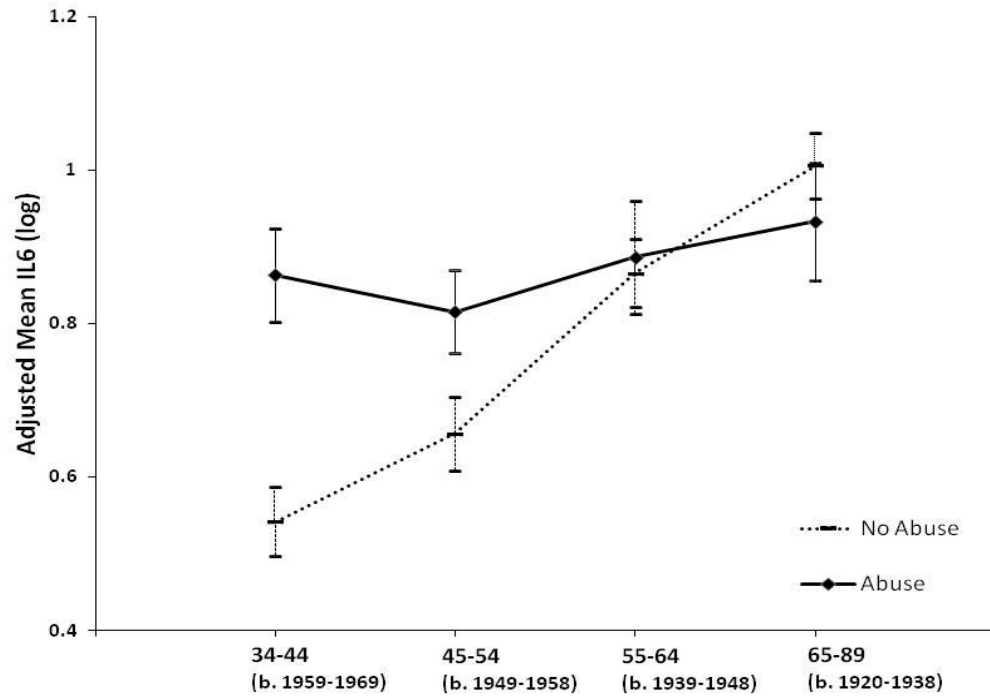**Figure 3-1 IL-6 Mean Levels by Abuse and Age Groups (birth year)**

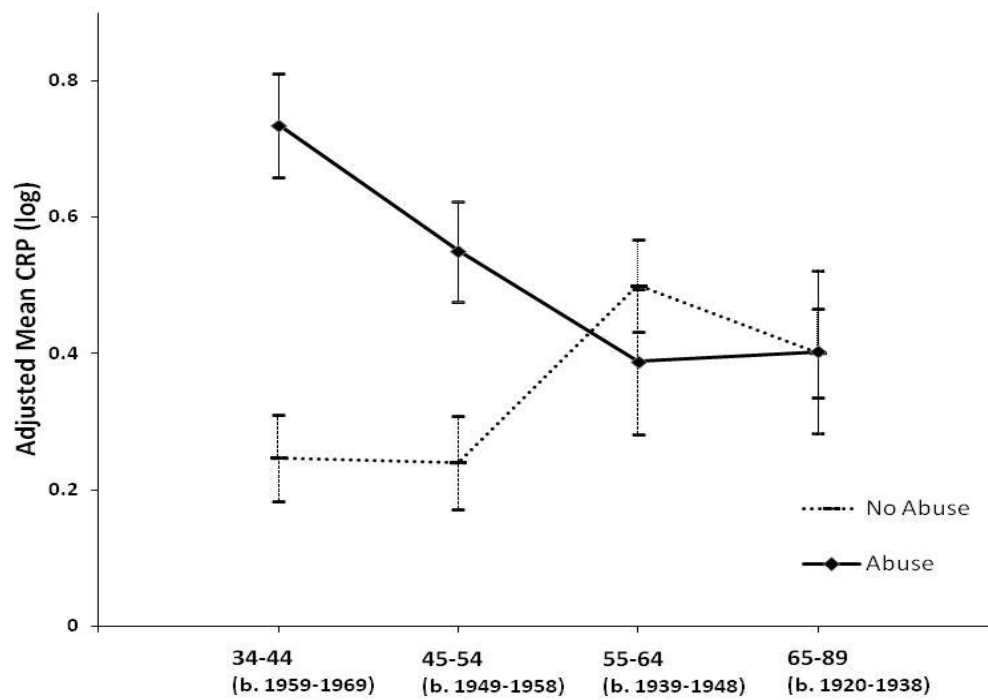**Figure 3-2 CRP Mean Levels by Abuse and Age Groups (birth year)**

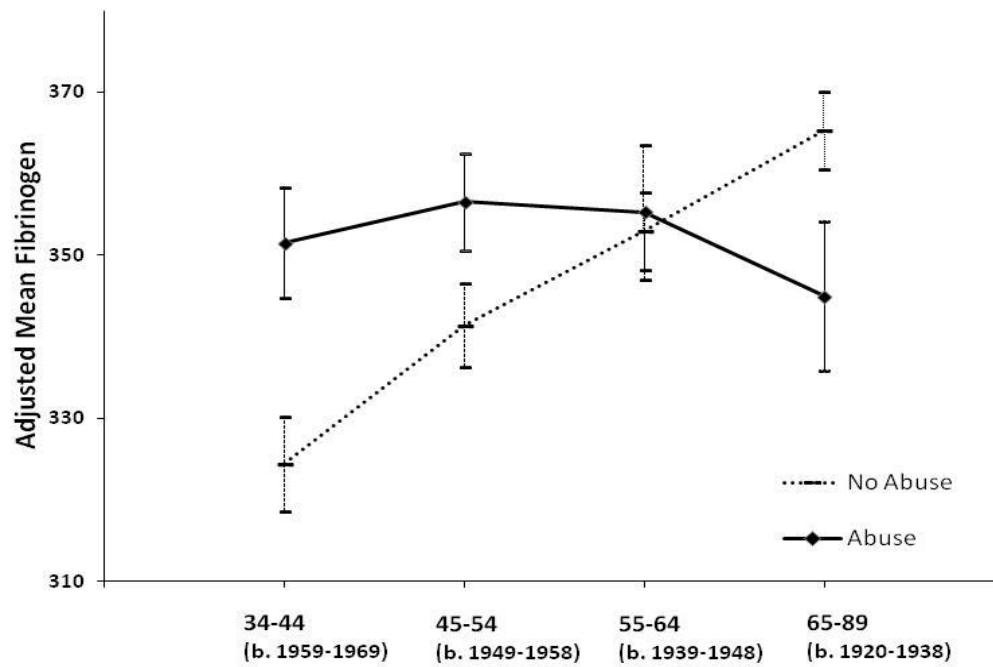**Figure 3-3 Fibrinogen Mean Levels by Abuse and Age Groups (birth year)**
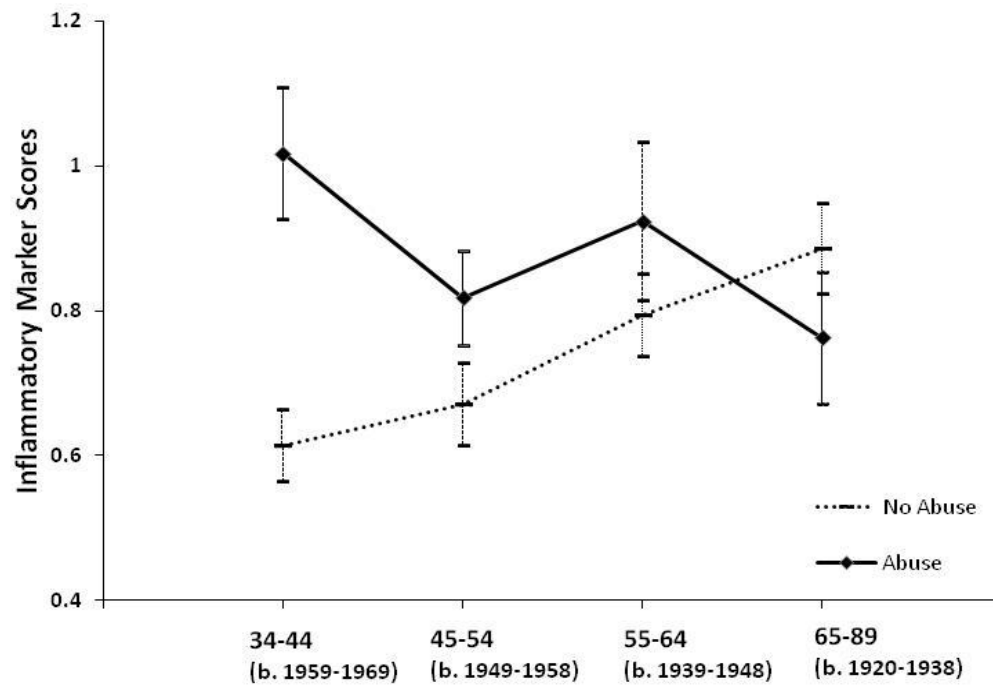
Figure 3-4 Summary Scores of Inflammatory Markers by Abuse and Age Group (birth year)

Chapter 5-Conclusions

Childhood abuse and neglect is a significant public health concern in the U.S. According to NCANDS, an estimated 702,000 children were determined to be victims of child abuse and neglect in 2009 across all states, and 1,770 children died directly due to such abuse and neglect (USDHHS 2010). Victims of childhood abuse are at greater risk of developmental and health problems over the life course (Child Welfare Information Gateway 2008). Although studies have documented psychosocial and behavioral pathways that link childhood abuse to adverse lifelong health outcomes, few studies have investigated physiological pathways and outcomes for victims of such abuse. My project was motivated by recent calls by health researchers to integrate biomedical knowledge with sociological perspectives to better understand health outcomes over the life course. Drawing on stress theories and life course approaches to health, my dissertation examined the long-term effects of childhood abuse on physiological dysregulation. I focused on ten biomarkers that indicate the health of multiple body systems (the HPA axis, the SAM axis, and the immune system). I applied an emerging theory in biomedical research (bidirectional cortisol abnormality) and used advanced measures of childhood abuse and abnormal cortisol levels. My study provides new evidence for why victims of childhood abuse exhibit physiological dysregulation and it offers methodological suggestions for both sociological and biomedical research.

Contributions

My project makes three methodological and conceptual contributions to contemporary research on childhood abuse and the long-term impacts of early life stressors on health outcomes. The first contribution involves my use of an innovative method, latent class analysis (LCA), to identify profiles of childhood abuse. I attempt to overcome the limitations of most childhood

abuse studies, which only examine an extremely broad or narrow set of measures of childhood abuse. These measures do not fully capture all the natures of childhood abuse, including its severity, frequency, and multifaceted subtypes. Using LCA, I identified the underlying heterogeneity of childhood abuse experiences and created profiles of childhood abuse characterized by a comprehensive combination of severity and type of abuses. These LCA classes allow us to understand better the distinctive profiles of childhood abuse for the full sample (five classes) as well as for men (four classes), and for women (five classes) separately, which would not have been discovered using a simpler measure of childhood abuse.

My second contribution is to apply new theories of bidirectional cortisol abnormality, to examine and explain how childhood abuse increases the risk of developing chronic diseases (allergies, asthma, and arthritis) in adulthood. Most prior studies have considered cortisol abnormality as uni-directional, examining only extremely high levels of cortisol. This focus might reflect, in part, the widespread use of allostatic load indicators, which typically operationalize high-risk cortisol levels as the top 25% of the distribution. By contrast, I use both the *top* and *bottom* quartiles of the cortisol distribution to explain the linkage between childhood abuse and its effects on an individual's risk of developing immune-related disorders. This novel approach can provide useful guidance about how to operationalize cortisol dysregulation for both biomedical and sociological research, and it shows how findings from uni-directional cortisol abnormality analyses might mischaracterize the association between childhood abuse and cortisol levels.

Regarding my third contribution, I pay close attention to the heterogeneous effects of childhood abuse on physiological dysregulation. I argue that gender and age might play important roles in explaining the heterogeneity. First, gender is a central component in understanding the nature of childhood abuse, coping strategies, and the development of diseases, yet previous studies have ignored the importance of gender when examining the effects of childhood abuse on physiological dysregulation. I explore gender differences in the profiles of childhood abuse and

test how each profile of childhood abuse is associated with physiological dysregulation differently for men and women. Second, many studies document the long-term effects of childhood abuse on poor health outcomes, yet few have evaluated whether these patterns differ by life course stage. Guided by life course approaches and selective mortality theory, my project investigates whether associations between childhood abuse and physiological dysregulation in adulthood vary across age groups.

Key Findings

Latent Classes of Childhood Abuse

Most abused children experience multiple types of abuse with varying degrees of severity and chronicity or frequency (Cicchetti and Toth 1993; Irving and Ferraro 2006). Given the potentially complicated features of abuse, latent class modeling is beneficial in identifying distinct groups of individuals with a characteristic history of childhood abuse. Using LCA with indicators from the Childhood Trauma Questionnaire (CTQ; Bernstein and Fink 1998), I found five classes of childhood abuse in the full respondents sample, each characterized by different combinations of types and severity of abuse. There are gender differences in profiles of childhood abuse. Women have five classes and the patterns of the classes are similar to those in the full sample. Yet, men have four classes.

Moreover, there are several gender differences in childhood abuse profiles which emerge in several ways. Women (42%) are more likely to report experiences of childhood abuse than men (26%). Among abused individuals, physical and emotional abuse are common for both men and women with different levels of severity, yet women are more likely than men to report high levels of emotional abuse. Sexual abuse is also more common for women than men. For women, there are two different forms of sexual abuse: one consists of high levels of sexual abuse combined with other high levels of abuse, and the other is made of high levels of sexual abuse

combined with other low levels of abuse. For men, there is only a single form of sexual abuse, which occurs along with high levels of emotional abuse and medium levels of physical abuse. My findings are consistent with those in previous studies, which were based on both self-reported and official records of childhood abuse, indicating a higher prevalence of sexual abuse for women than for men (Dube et al. 2005; Sedlak et al. 2010). Nonetheless, I extended previous research by revealing comprehensive profiles of childhood abuse, which differ by gender. Lower social and economic status for women, compared to men, may increase the chance of being exposed to such abuse.

Cortisol Abnormality as a Potential Mediator Linking Childhood Abuse to Immune-Related Disorders

The function of the HPA axis for victims of childhood abuse has been studied intensely in the areas of childhood abuse and physiological dysregulation. Studies suggest that abnormal levels of the stress hormone cortisol might be one of the plausible mechanisms that accounts for the association between childhood abuse and stress-induced diseases, such as asthma and arthritis (Fries et al. 2005). Recently, theories propose that cortisol abnormality might be bidirectional (hypercortisolism and hypocortisolism), and that distant traumatic stress (e.g., sexual abuse in childhood) is likely to be associated with hypocortisolism in adulthood (Trickett et al. 2010). Since cortisol is one of the most well-known anti-inflammatory hormones that suppress inflammation processes, a continued lack of cortisol might lead to abnormal immune functions and may eventually increase vulnerability to immune-related disorders (Heim et al. 2000a). Despite the importance of these theories in understanding the health outcomes for victims of childhood abuse, I know of no clinic- or population-based study that assesses either: 1) the association between childhood abuse and bidirectional cortisol abnormality or 2) the mediation

effect of abnormal levels of cortisol on the association between childhood abuse and immune-related disorders.

Using latent classes of childhood abuse, I examined whether childhood abuse is associated with cortisol abnormality (hypocortisolism or hypercortisolism). I also evaluated the extent to which high or low levels of cortisol mediate the linkage between childhood abuse and elevated risk of immune-related disorders (allergies, asthma, and arthritis). There are three key findings. First, victims of childhood abuse, compared to non-victims, have an elevated risk of all three immune-related disorders at midlife. Sexual abuse especially plays an important role in increasing the likelihood that adults will have all three immune-related disorders. Second, compared to non-victims, victims of childhood abuse are more likely to display hypocortisolism rather than hypercortisolism. Particularly, individuals who experienced high levels of physical, emotional, and sexual abuse have significantly lower cortisol levels than those who did not experience childhood abuse. Finally, there is some evidence that hypocortisolism partially mediates the association between childhood abuse and immune-related disorders. Victims of all three types of high levels of childhood abuse, compared to non-victims, have an increased risk of all three immune-related disorders. A part of this association is partially explained by hypocortisolism. However, the indirect effect explained by of hypocortisolism is only significantly predicts the likelihood that an individual will develop arthritis and allergies (not asthma), and the size of this mediation effect is small, explaining just of 7% for arthritis and 11% for allergies.

Overall, my findings suggest that the nature of childhood abuse determines an individual's risk of developing immune related-disorders. My findings support emerging theories related to stress, hypocortisolism, and immune-related disorders, providing novel evidence about the association between early life stressors and chronic diseases mediated by hypocortisolism in

population-based data. My approach to the operationalization of cortisol abnormality provides useful information for both biomedical and sociological research.

Childhood Abuse and Metabolic Syndrome in Men and Women in Midlife: Poor Sleep Quality and Stress-Induced Eating as Potential Mediators

MetS, which is characterized by a combination of metabolic disturbances, such as abdominal obesity, glucose intolerance, high blood pressure, and high bad and low good cholesterol levels (Alberti et al. 2006), is a key risk factor for the leading causes of death in the U.S. (i.e., cardiovascular disease, coronary heart disease, and stroke) (Ford 2005). Research indicates that childhood abuse is associated with an elevated risk of metabolic disturbance as well as psychosocial and behavioral conditions (e.g., sleep and eating problems), which eventually lead to an increased risk of developing MetS. Gender is an essential component of understanding the association between childhood abuse and MetS due to gender differences in the characteristics of childhood abuse, coping skills, and the prevalence of MetS. There are few studies that document the extent to which psychosocial and behavioral mediators explain the association between childhood abuse and MetS. To my knowledge, no study explores the role of gender in understanding the association as I have done in this dissertation.

Using latent classes of childhood abuse for men and women, I examined whether childhood abuse is associated with MetS (MetS diagnosis and cumulative numbers of MetS components). I also evaluated the extent to which poor sleep quality and stress-induced eating mediate the linkage between childhood abuse and elevated MetS for men and women. I found that not all individuals who experienced childhood abuse are more likely to have MetS. For women, the experience of high levels of emotional/physical/sexual abuse increases their risk of developing a MetS diagnosis, while for men, high levels of emotional abuse and medium levels of physical abuse, without high levels of sexual abuse, increases the number of MetS

components. Both men and women who experienced childhood abuse are likely to have elevated

levels of both sleep and eating problems. Sleep problems are more common than eating problems

for both genders. Yet, neither sleep nor eating problems significantly mediate the association

between childhood abuse and MetS for either men or women.

My findings suggest that some types of childhood abuse are significantly associated with

the risk of developing on MetS, which may have significant public-health implications. It is

important to understand gender differences in the profiles of childhood abuse because for women,

sexual abuse with high levels of other forms of abuse is associated with increased risk of

developing MetS, but for men, sexual abuse does not necessarily increase their risk.

Effects of Childhood Abuse on Elevated Markers of Inflammation in Adulthood: Do the

Effects Differ Across the Life Course Stages?

Research indicates that victims of childhood abuse are particularly susceptible to

developing certain disorders in childhood and/or adulthood, including autoimmune disorders,

osteoarthritis, allergies, and asthma in childhood and/or adulthood (Dube et al. 2009; Felitti et al.

1998; Fuller-Thomson et al. 2009). Stress-induced immune dysfunction and elevated levels of

inflammation are considered to be mechanisms explaining the high prevalence of such disorders

(Kiecolt-Glaser et al. 2002). An emerging body of research finds that childhood abuse is

associated with elevated markers of inflammation in both young adulthood (Danese et al. 2007;

Taylor et al. 2006) and midlife (Slopen et al. 2010). Research also indicates that psychological

and behavioral factors (e.g., obesity and physical exercise) partially explain the associations

between childhood abuse and elevated markers of inflammation. Despite the importance of

timely, efficient interventions to eliminate poor health outcomes for victims of childhood abuse,

to my knowledge no study has investigated whether the effect of childhood abuse leads to

different health outcomes at different stages of the life course, in particular for individuals in later midlife and old age.

Selective mortality and "age-as-leveler" theories suggest that the effects of socioeconomic status (SES) on health vary by life course stages (House et al. 2005). These perspectives propose that differences in SES-based health disparities are largest at middle age and then narrow and disappear in later old age. This attenuation may reflect premature death among individuals with low SES, or it might reflect the biological fragility of old people regardless of their SES. Given that victims of childhood abuse, compared to non-victims, are less likely to achieve high SES (Currie and Widom 2010), there may exist age variations by selective mortality.

Guided by life course approaches and selective mortality theory, I investigated associations between childhood abuse and levels of inflammatory biomarkers: interleukin (IL)-6, C-reactive protein (CRP), and fibrinogen for adults (ages 34-84), and I examined the extent to which associations between childhood abuse and levels of inflammatory markers vary across age groups (ages 34-44, 45-54, 55-64, and 65-84). I also evaluated the extent to which these associations are mediated by four plausible pathways: sleep problems, body mass index (BMI), perceived stress, and family social ties ("family affectual solidarity"). I found significant main effects and age-by-abuse interaction effects on levels of inflammatory makers, yet the main effect emerges only when the interaction term is included. That is, the effects of childhood abuse on inflammatory markers differ by age groups. In the younger age groups (ages 34-44 and 45-54), victims of childhood abuse, compared to non-victims, have elevated markers of inflammation for levels of all three inflammatory markers, while there are no significant effects of childhood abuse on any inflammatory markers in the older age groups, (ages 55-64 and 65-84), in particular in the oldest age group (65-84). Thus, the findings would not have been detected and the unique risk factors of the young groups would not have been observed without stratifying the sample by age.

I also found that adult mortality rates are greater for victims of childhood abuse than non-victims, which provides evidence that selective mortality might contribute to a reduced difference in of levels of inflammatory markers between victims and non-victims in the older age groups. High BMI, poor sleep quality, and low family social ties partially explain why the experience of childhood abuse increases levels of inflammatory markers. Overall, my findings suggest that life course stages should be considered when studying the effects of childhood abuse on levels of inflammatory markers. Interventions to prevent the effects of childhood abuse on adult inflammation need to target younger adults to help reduce their risk of developing chronic diseases (e.g., cardiovascular diseases) through elevated markers of inflammation.

Limitations

This project has three major limitations. First, causality cannot be definitively ascertained. Although MIDUS is a nationally representative longitudinal study, the biomarker data are cross-sectional and were collected at the end of the last MIDUS survey (2004-2009). Thus, it is not possible to conclude that a strong causal association exists between physiological dysregulation and the development of chronic diseases or to determine the direction of that association. Regarding the association between cortisol abnormality and immune-related disorders, it is possible that corticosteroid medications that individuals with immune-related disorders have taken might alter the HPA axis, eventually resulting in a reduced amount of cortisol secretion (Dluhy 1998). Future studies should explore these relationships with data collected at various time points throughout childhood and adulthood to reveal the causal pathway.

Second, retrospective self-reports of childhood abuse may be susceptible to recall bias (White et al. 2007). Since the questions about childhood abuse in MIDUS were asked in midlife or old age and require retrospective evaluations of experiences that may have occurred as much as 50 years earlier, one might expect that the reliability of the retrospective reports of childhood

abuse might be low. Prior studies have found an inconsistency in the self-reporting of physical

abuse between when respondents were adolescents and young adults (White et al. 2007). Other

studies suggest that current mood disorders might distort the memory of adversities that

individuals experienced in childhood (Widom and Morris 1997). On the other hand, some studies

assert that the memories of particular childhood experiences (e.g., positive relationships, negative

events, and parental discipline) are highly stable (Yancura and Aldwin 2009) and fairly accurate

(for a review, see Hardt and Rutter 2004). To confirm the reliability of the retrospective reports of

childhood abuse in MIDUS, I conducted supplementary analyses and found both a strong

correlation (.76) and consistency (84.5%) between the reports of physical abuse that were

measured across the 10-year gap at of MIDUS I and MIDUS II. I also found that mood disorder

(e.g., depression) does not significantly affect the repeated reports of physical abuse over the 10-

year span. Therefore, it is reasonable to assume that biased findings due to self-reported

childhood abuse are minor in my study.

Third, the relatively small sample prevents the exploration of more fine-grained subgroup

patterns. For example, when analyzing the age-by-abuse interaction effects on inflammation, I

combined all four abuse groups, generated by the LCA, into one group, named "abuse." Thus, the

measure "abuse" does not reflect different severity and multiple subtypes of childhood abuse

experiences or the severity of abuse. In addition, due to the relatively small size of the sample

across age groups, I merged all the individuals who were 65 or older into one group (ages 65-84).

That merger does not allow me to evaluate whether the effects of childhood abuse on

inflammation vary by age within the oldest group (ages 65-84).

In addition, the small sample size might affect the statistical power when applying

subsequent analyses with the LCA classes of childhood abuse. Specifically, some of the latent

class groups (e.g., high emotional/physical/sexual abuse) include less than 50 individuals. Since

biomarkers are sensitive to various controls, including demographics, health conditions,

medications, and health behaviors, I include several controls to eliminate the possibility of potential spurious associations between childhood abuse and outcome variables through confounding variables. These factors might also influence the power of a statistical test. A larger sample would certainly improve the statistical power and allow me to better understand group differences. To gain more confidence in these findings, future studies are needed to replicate my studies in should use larger samples.

Future Research Directions

Due to the limitations of the childhood abuse measure, CTQ, I only focus on subtypes and severity of childhood abuse. Other aspects of childhood abuse, such as the developmental period (timing) and the relationships between the abuser and the abused, might play important roles in determining the risk of developing physiological dysregulation. First, the timing of childhood abuse might determine whether childhood abuse directly influences physiological dysregulation. Research indicates that the degree of sensitivity and plasticity in parts of the brain (e.g., the hippocampus) that regulate the HPA axis, is greater in infancy and toddlerhood than in other life course stages (Lupien et al. 2009). Exposure to childhood abuse from the early period might lead to permanent changes in HPA activation, as well as to the dysregulation of stress hormones (Heim et al. 2000b).

Second, relationships between the abused and the abuser might significantly influence cognitive, emotional, or social development for victims of childhood abuse. Attachment theory (Bowlby 1988) suggests that infants and children develop basic social skills through interactions with their primary caregiver. When children are abused by a primary caregiver, they might fail to develop such skills and psychological strengths, including strong self-esteem and self-control. That failure can ultimately contribute to an unregulated response to stressors and to dysregulation

of body systems. Therefore, future studies need to consider even more diverse variables related of childhood abuse (e.g., timing of abuse and relationship to perpetrator) than I do.

Victims of childhood abuse also may be at elevated risk of experiencing secondary stressors over the life course, which might play key roles in their subsequent risk of developing physiological dysregulation. Cumulative inequality theory (Ferraro and Shippee 2009) proposes that adults who experience adversities (e.g., school dropout and child abuse) in early life are more likely to experience adversities (e.g., job loss) in later life than those who do not experience them. Victims of childhood abuse, compared to non-victims, are more likely to experience adversities in later life. Therefore, cumulative adversities and stressors that victims experience should be considered to comprehend lifelong health consequences for victims of abuse. In addition, certain adversities might have a more negative influence on health than others. Although cumulative adversities have a graded association with adult poor health in adulthood (Turner and Lloyd 1995), it is possible to expect that certain traumatic events (e.g., sexual assault, combat experience, and death of a child) might more pervasively affect health than others (e.g., job loss and divorce). Therefore, future research needs to investigate these key aspects of life adversities.

Strengths and Limitations of Using Biomarkers in Biosociological Issues in Health

Over the past decade, there has been a growing tendency for social scientists to include biomarkers in large population-based surveys. By incorporating biological and sociological data, researchers expect to address many new issues related to social determinants of health (National Research Council 2010). While working on my project, I recognized several strengths and limitations associated with using biomarkers to investigate the effects of childhood abuse on physiological dysregulation.

Biomarkers have been very useful in my own study of the effects of childhood abuse on physiological dysregulation. They measure a wide range of physical functions, reflecting disease

conditions which might be difficult to capture with measures of self-reported health. For example, inflammatory conditions, which I found to have significant associations with childhood abuse, cannot be measured without biomarkers, such as IL-6, fibrinogen, and CRP. I also found there were significant discrepancies in the prevalence of diabetes between a subjective measure of health and the biomarker data (glycosylated hemoglobin, HbA1c). While approximately 13% of respondents reported having diabetes, HbA1c shows that 35% of the respondents meet the criteria for having a diabetic condition (HbAlc $\geq$ 6.0%). The difference may be attributed to many respondents being unaware that they have developed diabetes. If I had relied on a subjective measure of diabetes, I might have underestimated the association between childhood abuse and MetS. Using biomarkers, I also can test the associations between childhood abuse and physiological functioning in multiple body systems (the HPA axis, the SAM axis, and the immune system). I found that the associations between childhood abuse and physiological dysregulation vary by body system. Gender and age explain some of the variation.

The use of biomarkers in sociological studies also presents several difficulties. Many biomarkers do not have standard cut-off values that can be used as evidence of physiological dysregulation, such as a disease condition. For example, there are no clear guidelines for operationalizing hypocortisolism using 12-hour urinary cortisol. Guided by allostatic load measures (e.g., high-risk 12-hour urinary cortisol levels at the top 25% of the distribution), I operationalize the top and bottom 25% as hypercortisolism and hypocortisolism, respectively. This operationalization causes a conceptual issue in that half of the respondents are categorized as having abnormal levels of cortisol. I strongly encourage biomedical research to devote effort to determining clinical cut-offs or abnormal ranges which represent physiological dysfunction.

In addition, although numerous clinical studies have reported that physiological dysregulation varies by demographic characteristics (e.g., age and gender); most studies are limited to small samples in clinical settings. Findings from such studies might not be

generalizable to the population and might not offer criteria for determining how abnormal aging varies by sociodemographic characteristics in one population, compared to other populations. Except for Yang and Kozloski's (2011), there is little based on population-based data that investigates whether the distributions and patterns of physiological dysregulation in multiple body systems vary by gender, race, and/or age. Given the dearth of knowledge, I had difficulties in evaluating whether a level or pattern of physiological dysregulation (e.g., IL-6 and fibrinogen) for victims of childhood abuse, compared to non-victims, is abnormal. I look forward to more population-based studies that investigate the extent to which physiological dysregulation varies by gender and race across stages of the life course.

Policy Implications

Despite the detrimental effects of childhood abuse on physiological dysregulation, I find that not all abused individuals are at greater risk of developing physiological dysregulation. Some individuals who experienced childhood abuse do not develop cortisol abnormality, MetS, or elevated markers of inflammation. Resilience theories (Masten et al. 1990) propose several possible reasons why adversities might not produce negative outcomes. According to Masten and colleagues (1990, p.426), resilience indicates "the process of, capacity for, or outcome of successful adaptation," in threatening environments; resilience is fostered by protective factors that moderate the effects of an individual's vulnerability to harmful environments. Protective factors include both an individual's characteristics (e.g., optimism, hope, and altruism) and general life circumstances (e.g., having access to educational and social welfare services) (Mrazek and Mrazek 1987). Studies identify a number of protective factors that may contribute to resilience for victims of childhood abuse, such as high self-esteem, positive coping strategies, perceived social support from family and peers, neighborhood stability, and access to safe schools and to adequate health care (Fraser and Terzian 2005; Tremblay et al. 1999).

In my project, I find that coping resources, such as family social ties, play an important role in reducing the risk of developing physiological dysregulation. Family social ties, measured by "family affectual solidarity," attenuate the effect of childhood abuse on elevated markers of inflammation. Although non-victims compared to victims of childhood abuse have stronger family social ties in the younger cohorts (ages 34-64), I do not find differences in the quality of such social ties in the oldest cohort (ages 65-84). Previous research indicates links a high quality of social ties is linked with to positive physical and mental health outcomes in adulthood (Kawachi and Berkman 2001; Walen and Lachman 2000). This might be one plausible reason why I do not find the childhood abuse leads to elevated markers of inflammation in old age.

Some research suggests that strong social involvement might modify the effects of childhood abuse on physiological dysregulation (Gunnar and Quevedo 2007). After receiving 10 weeks of supportive foster care, children with a history of childhood maltreatment showed normalized levels of cortisol (Dozier et al. 2006). Other research indicates that strong social ties help individuals achieve healthy behaviors or conditions, such as a healthy BMI, exercising, getting physical check-ups, and not smoking (Grzywacz and Marks 1999). These findings suggest that social ties might work as a buffer against the impact of childhood abuse on physiological dysregulation. Therefore, possible interventions might include training foster parents to provide sensitive and responsive care and providing programs in which victims of childhood abuse learn how to develop social skills and to improve social ties.

In addition, positive coping behaviors might reduce abused victims' propensity to develop physiological dysregulation. Research indicates that victims of childhood abuse, compared to non-victims, are more likely to engage in unhealthy negative coping behaviors (e.g., smoking, drinking, and binge eating), which might eventually lead to poor health outcomes in adulthood. Interestingly, I find that a group of men who experienced severe sexual abuse did not develop MetS. Compared to other abused men, they are less likely to use eating as a coping

behavior in response to stress and are less likely to smoke. The men in this group might use positive coping strategies in adulthood, which might reduce their risk of developing MetS. Moreover, I find that poor sleep quality and high levels of BMI, partially explain why the victims of childhood abuse have increased levels of inflammation. Therefore, to mitigate the adverse consequences of childhood abuse, I suggest that targeted interventions help victims of childhood abuse to reduce risk factors and develop healthy coping behaviors. In addition, I hope that my findings and suggestions will encourage fellow researchers to explore more fully how the experience of childhood abuse affects both mind and body of victims, and that an improved understanding will increase the societal well-being of individuals who experienced childhood abuse.

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