BACKGROUND LIFE STRESS, CARDIOVASCULAR RESPONSES TO LABORATORY STRESS, AND HEALTH OUTCOMES IN ADOLESCENTS AND YOUNG ADULTS WITH AND WITHOUT A HISTORY OF FUNCTIONAL ABDOMINAL PAIN

By

Grace D. Shelby

Dissertation
Submitted to the Faculty of the
Graduate School of Vanderbilt University
in partial fulfillment of the requirements
for the degree of
DOCTOR OF PHILOSOPHY
in
Psychology

December, 2012

Nashville, Tennessee

Approved:

Professor Lynn Walker

Professor Stephen Bruehl

Professor Craig A. Smith

Professor Bruce Compas

I dedicate this dissertation to those who have indelibly impressed upon my life, especially…

to Hannah and Sam Burrell, in loving memory, for inspiring a spirit of generosity, striving, and selflessness in my parents and our family;
to my cherished mother, Grace, father, Gary, and brother, Garien, for your unwavering support, sacrifice, humor, and encouragement and for inspiring me to find joy and passion in all I do as I give unto others following in your shining examples;
to my beloved Willis for your loving unyielding support, giving spirit, and calm patience;
to my dear friends Kezia and Ashley for your wonderful and caring companionship;
to my many outstanding early mentors and teachers, especially Dr. Beverly Thorn and Colonel Bryan Bennett, who have balanced support with challenge in nurturing my development;
to my esteemed past and current supervisors who have fostered my professional growth;
to my current colleagues and young faculty supporters for your continual encouragement.
I am indebted to you all.

ACKNOWLEDGEMENTS

This work would not have been possible without the support of R01 HD23264 (Lynn S. Walker, P.I.) from the National Institute on Child Health and Development, Vanderbilt Kennedy Center (P30 HD15052), Vanderbilt Digestive Disease Research Center (DK058404), and the Vanderbilt CTSA (1 UL1 RR024975). I was also supported in part by T32-MH18921.

It is with great pleasure that express my gratitude to those with whom I have had the honor to work during this and other related projects. I owe a debt of sincere gratitude to my research advisor, Dr. Lynn Walker, whose tremendously industrious support in providing expert research guidance and collaboration has encouraged me to advance my work in this and other research pursuits. I would like to recognize my committee, Drs. Craig Smith, Stephen Bruehl, and Bruce Compas. I am grateful to have had continually supportive committee members who provided expertise and advice with a spirit of encouragement. I would also like to acknowledge all the students of the Walker lab whose work over the years has made this research possible as well as the gracious participants who took part in this research.

I am eternally grateful to those who have been so important to me in this pursuit. I would foremost like to express my deepest gratitude to my dear parents, brother, and significant other, whose unyielding and unending support in every way carried me through this and so many other endeavors. It is with the utmost gratitude that I thank my loved ones, valued mentors and teachers, supervisors, colleagues, and dear friends who have supported my journey to this point. I wholeheartedly appreciate each person I have been blessed to have help me along this path for their contributions to and positive influences on not only this project but the course of my personal and professional development. For this and more, I have endless gratitude.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER I

INTRODUCTION

Functional abdominal pain (FAP) is one of the most common recurrent pain conditions in children and adolescents and is associated with high levels of somatic complaints, functional disability, school absences, and health service use (Walker, Garber, & Greene, 1994; Walker, Garber, Van Slyke, & Greene, 1995). Medical evaluations of abdominal pain aim to rule out evidence of organic disease that might explain patients' symptoms (Boyle, 1997; Hyams, et al., 1995; Walker, et al., 2004). Without structural or biochemical abnormalities associated with their pain, patients are considered to have medically unexplained or "functional" abdominal pain (Drossman, 1998). The majority of these patients meet Rome III symptom-based criteria for a functional gastrointestinal disorder (FGID) such as irritable bowel syndrome (IBS) or functional dyspepsia (Baber, Anderson, Puzanovova, & Walker, 2008).

Despite the absence of identifiable disease, a sizeable proportion of youth with FAP experience frequent, disabling pain and associated emotional and somatic symptoms that continue into adolescence and adulthood. Recent investigations have found that, among youth with recurrent abdominal pain followed for 5-10 years, approximately one-third reported abdominal pain at follow-up (Gieteling, Bierma-Zeinstra, Passchier, & Berger, 2008; Walker, Dengler-Crish, Rippel, & Bruehl, 2010). FAP has also been associated with comorbid psychological and psychiatric symptoms such as greater anxiety symptoms and disorders and, to some extent, depressive symptoms (Campo, et al., 2001). Given that FAP is by definition not explained by an organic cause, a biopsychosocial perspective is often applied to understand how

factors such as life stress and altered physiology might interact to affect symptom onset, exacerbation, and maintenance in patients in FAP (Drossman, 1998; Drossman, et al., 1999; Hyams & Hyman, 1998).

In the remainder of this chapter, review of relevant theoretical and empirical literature supporting the moderating role or the potentially causal role of physiologic processes in the relation between life stress and health outcomes is provided. First, empirical support for life stress and health outcomes is reviewed. Next, factors affecting this relation are described, with an emphasis on physiological responses as a potential individual difference or causal factor in the relation between background life stress and health outcomes. Review of these literatures as they pertain to functional abdominal pain is provided in each of the aforementioned sections. The rationale for the current study is then outlined. Finally, specific hypotheses for the current study are presented.

Background Life Stress and Health in FAP

The empirical literature on FAP supports a prominent role of life stress (Burke, Elliott, & Fleissner, 1999; Chang, 2011; Mayer, Naliboff, Chang, & Coutinho, 2001). Events in human life can be described as stressors when they are perceived as threatening (Ehlert & Straub, 1998), and such stressors can encompass a variety of naturally occurring problems. Stressors can range from time-limited “acute stressors” or life-threatening, major critical “traumatic" life events (e.g., natural disasters, abuse, violence) to daily hassles to open-ended, enduring “chronic stressors” of life conditions (e.g., poverty). Stressors not only range in duration from short-lived to episodic to chronic, but also vary in magnitude of burden with some perceived as more threatening than others. However, a common approach in research has been to assess life stress with life event

questionnaires, which generally omit abuse, violence, and neglect, and rarely assess the duration of stressor exposure, the nature and duration of subsequent related stressors, or the threat value of stressors including factors such as the valence, magnitude, and meaning of stressors. Therefore, in this paper, the term "background life stress" is used to broadly encompass the variety of life events faced by individuals (Gump & Matthews, 1999). Despite its drawbacks, the construct of background life stress, as assessed by life events questionnaire measurement that identifies the accumulation of various stressful life events, has received much empirical attention. Such methods have been employed in studies of FAP in an effort to determine the extent to which FAP is characterized by a psychosocial context of high background life stress.

Background life stress is generally thought to be greater among individuals with FAP in comparison to healthy controls. While some studies have found no differences in background life stress between FAP and other groups (e.g., McGrath, Goodman, Firestone, Shipman, & Peters, 1983; Walker, Garber, & Greene, 1993; Walker & Greene, 1991b; Wasserman, Whitington, & Rivara, 1988), the preponderance of more recent studies have shown significantly higher levels of background life stress in patients with FAP compared to healthy controls (Blanchard, et al., 2008; Boey & Goh, 2001; Creed, Craig, & Farmer, 1988; Greene, Walker, Hickson, & Thompson, 1985; Liakopoulou-Kairis, et al., 2002; Robinson, Alverez, & Dodge, 1990; Walker, Garber, Smith, Van Slyke, & Claar, 2001; Walker, Guite, Duke, Barnard, & Greene, 1998; Whitehead, Crowell, Robinson, Heller, & Schuster, 1992).

Cross-sectional and longitudinal prospective investigations have evaluated the relation of background life stress to health outcomes in youth with FAP (Mayer, et al., 2001). For instance, Walker et al. (2001) found that daily stressors more strongly predicted somatic symptoms in children with FAP than in healthy controls. The authors concluded that children with FAP may

be more likely to respond to background life stress with somatic symptoms than are healthy children. Background life stress has also been associated with increased disability days and medical clinic visits in those with FAP (Whitehead, et al., 1992).

Moreover, background life stress has been linked to the onset and maintenance of abdominal pain, disability, and illness in FAP patients. There has been support for reciprocal relations between background life stress and symptom exacerbations in FAP (Blanchard, et al., 2008). Several studies have indicated greater life stress preceding the development of FAP (Creed, et al., 1988; Ford, Miller, Eastwood, & Eastwood, 1987; Gwee, et al., 1999; Nicholl, et al., 2008; Robinson, et al., 1990). Additionally, prospective investigations have shown that family background life stress predicted symptom maintenance in FAP patients at 3 months (Walker, Garber, & Greene, 1991) and 1 year (Walker, et al., 1994) following patients' medical evaluation for abdominal pain. Whitehead et al. (1992) similarly showed with time-lagged correlations over 3 months that background life stressors were associated with subsequent bowel symptoms. Background life stress also contributed to greater illness severity, disability, and somatic symptoms in FAP patients at 1 year follow-up (Walker, et al., 1991, 1994; Walker & Greene, 1987) and at 5 year follow-up (Mulvaney, Lambert, Garber, & Walker, 2006). The presence of even a single chronic life stressor has been linked with subsequent symptom intensity (Bennett, Tennant, Piesse, Badcock, & Kellow, 1998; Jørgensen, et al., 1993) and poor improvement over a year later in individuals with FAP (Bennett, et al., 1998). Negative life events have also been linked with psychological outcomes such as the maintenance of anxiety symptoms at 3 months (Walker & Greene, 1991b). Importantly, the relation of background life stress to symptoms and other outcomes has been shown to be independent of measures of

psychological distress (Biggs, Aziz, Tomenson, & Creed, 2003; Gwee, et al., 1999; Locke, Weaver, Melton, & Talley, 2004).

Factors Influencing the Relation of Background Life Stress to Health

Positive associations between a variety of types of background life stress and a host of adverse physical and mental health outcomes have been well-documented (Clements & Turpin, 2000). However, across groups, variation in the level of background life stress in and of itself has not been sufficient to explain the variability in patients' health outcomes (Boyce, et al., 1995; Jemerin & Boyce, 1990). Explanations for the stress-illness relation have ranged from individual differences in psychological functioning and perceptions of stress to psychobiological models implicating physiological pathways (Clements & Turpin, 2000). Among the factors that may contribute to individual differences in outcomes, individual differences in biological and physiological susceptibility to stress or "stress reactivity" are being increasingly implicated in rendering some individuals more vulnerable or "predisposed" to the effects of psychosocial adversity on their health and illness (Boyce & Ellis, 2005; Boyce & Jemerin, 1990). In addition, physiological processes may be contributing mechanisms leading from stress to illness. These two possibilities are reviewed in the following sections.

Moderating Role of Physiological Reactivity and Recovery

Overview and Theoretical Framework

Both theoretical and empirical literatures suggest that background life stress may interact with other risk factors to increase individuals' vulnerability to stressful events and influence the

course of illness or disease (Compas & Phares, 1991; Taylor, 2010). Such a conceptualization is consistent with the diathesis-stress model, a theoretical model which proposes that certain factors may predispose individuals toward greater stress reactivity and that particular health outcomes may only appear in the face of adverse conditions such as background life stress (Belsky & Pluess, 2009).

Interindividual differences in physiological responses to environmental stress are thought to be established in childhood, and psychobiological stress reactivity may be a trait-like individual difference (Cohen, et al., 2002; McEwen, 2003; Repetti, Taylor, & Seeman, 2002). It is important to note that a number of other individual difference variables may influence physiological responding including genetic constitution, personality, and social support. Other noteworthy influences include trauma and temperamental anxiety. Abuse, trauma, and neglect early in life are widely established causes of longstanding biobehavioral and physiological alterations that render individuals who have endured such circumstances susceptible to numerous adverse outcomes (Anda, et al., 2006; Felitti, et al., 1998; Heim & Nemeroff, 2001).

Barring significant early life adversity or trauma, temperament has also been related to differences in physiological responding. Temperament reflects individual differences in reactivity, regulation, mood, and behavior. It has been described as a trait-like predisposition or style of responding to environmental challenge that is generally established early in life and is consistent over time (Boyce & Chesterman, 1990). "Uncertainty to the unfamiliar" represents a temperamental tendency to become behaviorally withdrawn and physiologically aroused (e.g., high heart rate, exaggerated startle response) in the face of novelty (Kagan, Reznick, & Snidman, 1988; Kagan, Snidman, & Peterson, 2000). Individual differences in behavioral inhibition or anxious temperament may in part explain how individuals with a low level of stress may have

heightened biobehavioral responses to a stressor while others have a higher threshold to respond (Boyce, Barr, & Zeltzer, 1992).

Whether resulting from early life experiences or temperamental anxiety, patterns of responding that reflect hyperresponsiveness to stressful life events have adverse physiological and health effects. "Reactive" individuals are thought to have heightened "biological sensitivity to context" (Boyce & Ellis, 2005) and mount persistent autonomic and other physiological responses to stressors, especially in the presence of high background life stress. Before further reviewing the role of heightened physiological reactivity in the stress-illness relation, the next section provides a brief overview of what is expected of human physiological systems in response to acute stress followed by a section regarding assessment of physiological responses to acute stressors.

Brief Overview of the Physiological Response to Acute Stress. A sharp, rapid rise in cardiovascular and other physiological and neural activity is expected to occur in reaction to an acute stressor. This represents the generally adaptive "fight or flight" response, as described by Cannon (1929), which engages the central and peripheral nervous systems. When an individual is presented with a stressor, perception of the stimulus as stressful, both cognitively (via the prefrontal cortex) and emotionally (via the limbic system), is needed to initiate the stress response circuit. The limbic system communicates with the hypothalamus, which coordinates the central nervous system and the body's organs to regulate the various functions of the body. This sets into motion a cascade of processes that comprise the autonomic nervous system (ANS) response.

The sympathetic nervous system (SNS) and parasympathetic nervous system (PNS) are branches of the ANS that direct an individual's automatic responses to stress. The SNS works

quickly in initiating the body's responses to stress by increasing blood pressure and heart rate, dilating the pupils, and slowing digestive and reproductive processes. Not long after the stress response is activated, the processes responsible for stress recovery are initiated by the PNS which controls the body's ability to recover from stress by decreasing blood pressure, slowing heart rate, and restoring processes such as digestion and reproduction.

Autonomic nervous system responses are brought to bear by way of neuroendocrine mechanisms (via the sympathetic-adrenal-medullary axis or SAM axis) and endocrine mechanisms (via the hypothalamic-pituitary-adrenocortical axis or HPA axis). The SAM axis is the part of the sympathetic nervous system of the ANS responsible for the fight or flight response, which is triggered by the release of epinephrine and norepinephrine by the SNS and which initiates behavioral arousal and cardiovascular responses. Because the SAM axis is a neuroendocrine-mediated mechanism involving both neural and endocrine tissues, stress stimulation of the SAM axis is much faster than the slower-acting response of the HPA axis, which represents a complex chain of endocrine hormones that are sent through the bloodstream. The HPA axis is conceptualized as a second wave of autonomic as well as immune responses following from the SAM responses.

This account of the biological processes associated with the stress response illustrates the influence of stress on the body and the involvement of multiple body systems. Among those with a propensity to react more frequently to stress due to heightened reactivity particularly under the conditions of greater life stress, frequent responding involves a cascade of physiological processes that one would expect would affect health and contribute to disease (Jemerin & Boyce, 1990).

Assessment of Physiological Responses to Acute Stress. Laboratory studies allow for further exploration of the physiologic processes linking background life stress with health outcomes under controlled conditions. In many studies, assessment of physiological stress responses is achieved via measurement of the body's responses to acute laboratory stress tasks, which generally have been designed to elicit particular physiological responses. Furthermore, responses to laboratory stress tasks have been associated with health and illness outcomes (Chida & Hamer, 2008). Measurements of the body's physiologic responses vary in nature and are "not created equal," with some responses initiated earlier than others. Additionally, some responses are elicited by one type of stressor but not another.

For several reasons including noninvasiveness of measurement, sensitivity of the measures, and the ability to indicate central stress regulatory processes, cardiovascular response has been a choice index of psychophysiologic responses to stress (Chida & Hamer, 2008; Jemerin & Boyce, 1990). Cardiovascular responses range from reactivity and recovery of heart rate and blood pressure to more novel indices of PNS involvement such as measures of vagal tone via heart rate variability (Porges, 2007). Because SNS responses are initiated quickly following exposure to a stressor, issues of timing of measurement are also a consideration. Cardiovascular responses such as blood pressure can be measured more quickly after stressor presentation, whereas HPA axis responses such as cortisol often take 20 minutes or more to appear.

It is important to also note that all laboratory stressors are "not created equal" and range from physical stimuli to speech tasks to cognitive and social stress tasks. Notably, some stressors elicit cardiovascular responses more readily than others. For instance, while used to elicit cardiovascular responses, the Trier Social Stress Test which consists of an anticipation period, delivery of free speech, and mental arithmetic in front of an audience has been most commonly

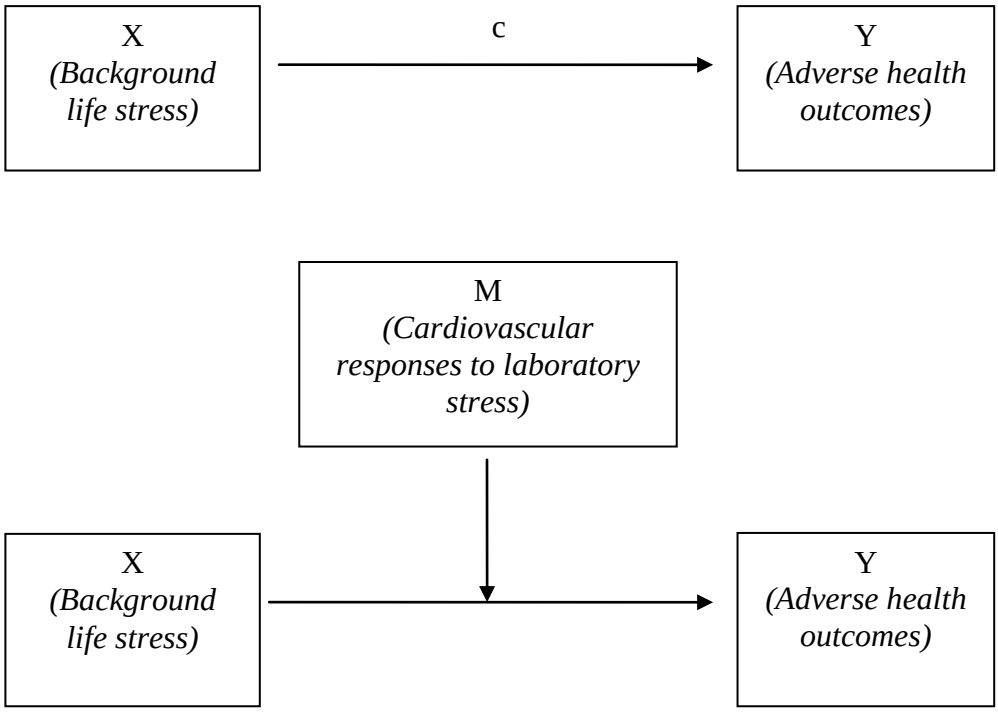
used to induce changes in cortisol and other neuroendocrine indicators (Dickerson & Kemeny, 2004; Kirschbaum, Pirke, & Hellhammer, 1993; Kudielka, Buske-Kirschbaum, Hellhammer, & Kirschbaum, 2004). The mental arithmetic task alone, such as serial subtraction, has frequently been used to elicit changes in blood pressure (Gerin & Pickering, 1995; Lassner, Matthews, & Stoney, 1994; Matthews, Woodall, & Allen, 1993) and has been shown to elicit larger blood pressure changes than mirror tracing and physical tasks such as hand-grip (Matthews & Stoney, 1988). The Social Competence Interview (Ewart & Kolodner, 1991) was specifically designed to induce cardiovascular responses, showed good test-retest reliability for doing so, and yielded blood pressure changes that exceeded those of other tasks including mental arithmetic. It also has the advantage of offering a more ecologically valid assessment of "real life" physiological responses (Ewart & Kolodner, 1991).

Assessments of cardiovascular reactivity have been found to be highly reliable which is thought to reflect the dispositional, stable nature of this construct (Manuck, 1994). While laboratory stressors are often lacking in ecological validity rendering them not clinically important in and of themselves, responses to laboratory stress tasks can serve as a marker of how vulnerable an individual is to acute stressors and associated illness risk by indexing the way an individual responds to ordinary demands (Chida & Hamer, 2008; Cohen, et al., 2002). Threshold to respond to stress, magnitude of response, latency to peak response, and recovery can represent individual differences in cardiovascular stress reactivity and recovery (Davidson, Jackson, & Kalin, 2000).

Conceptual Framework

Stable individual differences in physiological responding may be indexed via cardiovascular responses to laboratory stress tasks and may moderate the relation between background life stress and health outcomes. A conceptual schematic diagram of the simple effect of background life stress on health outcomes followed by a schematic diagram depicting the moderating effect of cardiovascular responses to laboratory stress responses are provided in Figure 1.

Figure 1. Schematic diagrams showing a simple effect and a moderation effect.



Empirical Literature on Cardiovascular Response as a Moderator

Studies empirically examining the interaction of background life stress and physiological stress reactivity in relation to various health outcomes are relatively rare, and studies conducted

in the last two decades have yielded findings in support of moderation. Assessing cortisol reactivity, Cohen et al. (2002) found that high reactors (i.e., high cortisol reactivity) to laboratory speech tasks who had greater negative life events had increased rates of upper respiratory illnesses than did high reactors who had fewer life events and low reactors in general. Additionally, low reactors were more likely to experience respiratory illness during high stress weeks than low stress weeks; high reactors did not demonstrate differences in respiratory illness as a function of weekly stress levels. With respect to cardiovascular responses, Boyce et al. (1995) found that environmental stress was related to higher rates of respiratory illness, but only among "psychobiologically reactive" children (i.e., those with higher cardiovascular and immune reactivity). Reactive children had higher rates of illness under high stress conditions and lower rates of illness in low stress conditions when compared with less reactive children. Clements and Turpin (2000) also found that cardiovascular reactivity moderated the relationship between life event scores and self-reported psychological distress such that life events scores predicted psychological symptoms only for high cardiovascular reactors. In some cases, physiological reactivity can be associated with a stress-buffering effect. For instance, El-Sheikh and colleagues (2001) found that children's vagal tone, an index of parasympathetic regulation of the heart, moderated the relation between marital conflict and health problems. Higher vagal tone buffered children against greater health problems related to greater exposure to marital conflict, particularly for boys.

The importance of individual difference variables in understanding FAP has been highlighted. It has been suggested that variability in symptoms and outcomes may be attributable to within-subject individual differences that may be obfuscated in between-group comparisons of background life stress between FAP and other groups (Walker, et al., 1998). For

instance, Walker and colleagues (2001) noted considerable variation among FAP patients in the strength of the association between daily stress and somatic symptoms; trait negative affect was a significant moderator, and the authors suggested the need for further research to identify individual difference variables that may moderate the association between stress and somatic symptoms.

Cardiovascular Response as a Moderator in FAP

Theoretical and conceptual understandings have supported individual differences in biological and physiological stress reactivity and susceptibility to stress in FAP. The sympathetic and parasympathetic branches of the ANS mediate bidirectional brain-gut communication largely through modulation of the third ANS branch, the enteric nervous system (Chang, 2011; Jones, Dilley, Drossman, & Crowell, 2005; Mayer, 2000; Mayer & Collins, 2002). As such, alterations in ANS functioning may play a role in FAP, and there has been increasing interest in not only visceral responses and motility but also central stress responses (Chang, 2011; Jones, et al., 2005; Tougas, 2000).

As previously noted, an individual may be predisposed to heightened reactivity to acute stress via such factors as inhibited temperament or anxiety, both of which characterize FAP. For example, Campo et al. (2004) documented higher levels of anxious or inhibited temperament in children with FAP compared with pain-free controls. It is thought that behavioral inhibition may be manifest in exaggerated reactivity to stress and delayed recovery (Boyce, et al., 1992). According to Chang (2011), "in a predisposed individual, sustained stress can result in enhanced responsiveness of central stress circuits, dysregulation of adaptive systems, and an increased vulnerability to develop functional disorders including IBS" (p. 761).

Empirical research on the potential moderating role of cardiovascular responses in the relation between background life stress and health outcomes in FAP, however, is sparse. Relatively few empirical studies to date have even examined physiological responses of any kind to acute stress in FAP. Of those that have, most have employed pain tasks and assessments using visceral sensitivity measures (e.g., Fichna & Storr, 2012; Mayer & Collins, 2002) while a few have examined HPA axis responsiveness (Chang, et al., 2008), but studies measuring cardioautonomic responses to stress and alterations in the central stress response in FAP are more limited (Chang, 2011).

Those studies which have examined the central stress response in FGIDs such as IBS have largely supported that dyregulations in ANS functioning exist but study findings have been mixed (Aggarwal, et al., 1994; Bach, Erdmann, Schmidtmann, & Mönnikes, 2006; Burr, Heitkemper, Jarrett, & Cain, 2000; Dufton, Dunn, Slosky, & Compas, 2011; Heitkemper, et al., 1998; Heitkemper, et al., 2001; Tillisch, et al., 2005; Waring, Chui, Japp, Nicol, & Ford, 2004). According to Chang (2011), "increased sympathetic nervous system activity and decreased parasympathetic nervous system activity are the most frequently noted differences when IBS patients are compared to healthy controls" (p. 764). Consistent with this, Dorn (2003) found that children with recurrent abdominal pain had higher stable heart rates and greater increases in systolic blood pressure than healthy controls following social and cognitive stress tasks. However, Dufton et al. (2008) found that some children with abdominal pain showed increases in heart rate in response to the social and academic laboratory stressors, whereas others showed a decrease in heart rate. Jørgensen et al. (1993), on the other hand, found that healthy controls had greater blood pressure and pulse rate increases than FAP following mental arithmetic. Additionally, no differences in heart rate variability have been found between an IBS sample and

healthy controls (Elsenbruch, Lovallo, & Orr, 2001; Mazurak, Seredyuk, Sauer, Teufel, & Enck, 2012).

It has been suggested that further research examine cardiovascular laboratory stress responses as a moderator of the relation between background life stress and health outcomes in FGIDs (Chang, 2011), but no known empirical studies have investigated this, particularly in FAP. Examination of the interaction of background life stress with cardioautonomic reactivity and recovery has the potential to inform not only how acute stress responses are viewed, but also to help identify individuals who are more vulnerable and those who are less vulnerable or resilient to the effects of stress on illness.

Mediating Role of Physiological Responses

Overview and Theoretical Framework

Recently, it has been suggested that the link between background life stress and health outcomes in FAP and other psychosomatic disorders results in part from a biological mechanism that mediates the relation between life stress and health (Ehlert & Straub, 1998; Walker & Greene, 1991b). Movement toward causal models including psychobiologic and physiological factors as the mechanism in the stress-illness relation has become increasingly considered as the physiologic effects of the stress response itself on pathophysiology and central stress response systems have been further elucidated (Schwartz, et al., 2003). Before reviewing theoretical and empirical literature, it would be appropriate to first provide a brief review of conceptualizations explaining the suspected pathways from stressors to physiological changes to disease.

Allostasis and Allostatic Load. Over 70 years ago, Hans Selye's seminal work recognized the role of positive and negative stressors in activating the body's physiologic systems. Yet, while these physiologic systems serve a protective function, Selye recognized that they also have damaging effects which can lead to disease. In the early 1980's, the "reactivity hypothesis" for cardiovascular functioning was put forth which posited that environmental demands such as background life stressors lead to physiological responses such as elevated blood pressure and heart rate that can contribute to cardiovascular disorders and illness risk (Dembroski, MacDougall, Slaats, Eliot, & Buell, 1981; Krantz & Manuck, 1984). In more recent years, McEwen and colleagues have put forth a conceptual framework that explains how chronic and recurrent background life stress may lead to physiological dysregulation of the body's regulatory systems which in turn leads to a host of diseases (Juster, McEwen, & Lupien, 2009; McEwen, 1998; McEwen & Lasley, 2002; McEwen & Wingfield, 2010). The body's response to stress has been termed "allostasis," which encompasses the manner in which the body's systems mobilize energy, interact with each other, and constantly change in order to maintain stability (McEwen, 1998; McEwen & Lasley, 2002; McEwen & Wingfield, 2010). Over time, prolonged or repeated responding as a result of chronic or recurrent stress yields an increased demand and burden on physiologic systems along with subsequent "wear and tear" on the body, termed "allostatic load" (Juster, et al., 2009; McEwen & Wingfield, 2010). As a result, long-lasting dysfunctional changes of behavioral and physiological stress systems are set in motion that can lead to disease and health-damaging behaviors (Evans & Kim, 2007).

The ability to mount the appropriate physiological responses and turn them off to foster the body's recovery can be impacted by a variety of factors including an individual's physical condition, genetics, behavioral and lifestyle choices, psychological factors such as the

individual's perception of the situation, and one's history of exposure to background life stress (McEwen, 1998). Allostatic load and the "wear and tear" associated with background life stress can be a predisposing factor for poor response to subsequent acute, stressful events which in turn may be associated with adverse health outcomes and disease.

There have been numerous suggestions in the literature that physiological reactivity to acute stress may be an underlying mechanism that mediates the relation between background life stress and health outcomes (Boyce & Ellis, 2005; Ellis, Essex, & Boyce, 2005; Evans & Lepore, 1992; Lercher, 1996; Luecken & Lemery, 2004; Schwartz, et al., 2003). The effects of biological dysregulation associated with stress responses are cumulative over time, and a temporal sequence of these effects has been advanced to aid in understanding the stress-disease process (Juster, et al., 2009). Stress hormones represent primary mediators. Secondary outcomes include alterations in reactivity of physiological systems such as cardiovascular and immune reactivity that may reflect sub-clinical pathology (Juster, et al., 2009). Finally, tertiary outcomes such as changes in basal cardiovascular functioning (Treiber, et al., 2001) as well as disease and disorder represent the final stage of "allostatic overload." In addition to support for increased reactivity, decreased reactivity would also be expected based on the principles of allostatic load and the potential for an inadequate response of some allostatic systems such that other systems have to respond more fervently to compensate (McEwen, 1998).

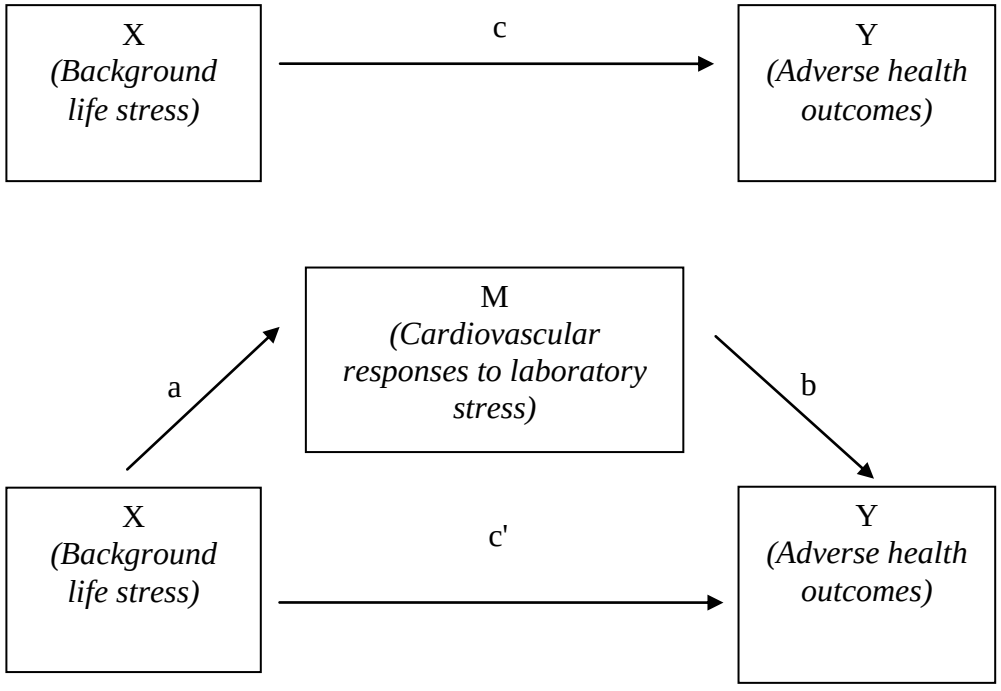
Conceptual Framework

Stressors not only activate body systems, but are thought to also have the capacity to change the reactivity of the central nervous system and other physiological systems of the body (McEwen, 2000). Individuals may become more likely to develop adverse outcomes when stress

responses are re-triggered or exacerbated in reaction to subsequent stressors (Mayer, et al., 2001). The various physiological markers of stress responses such as cardiovascular reactivity and recovery can be considered indicators of dysregulation of the body's regulatory physiological systems following stress (Evans & Kim, 2007; Juster, et al., 2009). Overall, physiological pathways may have the potential to explain how environmental stressors "get under the skin" and "get into the body," leading to adverse health outcomes (Barr, Boyce, & Zeltzer, 1996; Lupien, King, Meaney, & McEwen, 2001; Taylor, Repetti, & Seeman, 1997).

Figure 2 presents a conceptual schematic diagram depicting the simple effect of background life stress on health outcomes. Also presented is a schematic diagram depicting a mediational pathway linking background life stress, physiological responses to laboratory stress, and health outcomes.

Figure 2. Schematic diagrams showing a simple effect and a mediation effect.



Empirical Literature on Cardiovascular Response as a Mediator

A handful of studies have empirically tested a model of mediation with cardiovascular response to laboratory stress as the mediating factor. Lepore, Miles, and Levy (1997) found that cardiovascular reactivity to stress did not mediate the relation between chronic stress and illness, although individuals with more chronic background life stressors had exaggerated cardiovascular reactivity to acute challenges and reported more illnesses. However, Johnston-Brooks (1998) provided evidence that cardiovascular reactivity to laboratory stress mediated the relation between household density and medical illness in children and ruled-out cardiovascular stress reactivity as a moderator. Additionally, Gump, Matthews, and Räikkönen (1999) found that cardiovascular reactivity to laboratory stress mediated the relation between family background life stress and left ventricular mass, but only for Caucasian children and adolescents.

These investigations, however, tested mediation in cross-sectional study designs, a methodology that is fraught with issues of bias (Maxwell & Cole, 2007). Although many studies continue to test mediation with data from a single timepoint, longitudinal data are needed to accurately examine the meditational role of a given variable or factor (Cole & Maxwell, 2003). In the absence of such longitudinal designs, the pathways between the variables shown in Figure 2 can nonetheless be examined and offer a first step toward future prospective research that can more thoroughly examine the role of the factor of interest as a mediator.

With regard to the model proposed in Figure 2, the positive relation of background life stress to adverse health outcomes has been widely supported (pathway c'). Regarding Pathway a, empirical investigations in the last two decades have supported the role of background life stress in alterations of physiological responses to acute stress challenges and cardiovascular responses more specifically (for reviews, see Chida & Hamer, 2008; Gump & Matthews, 1999). However,

while background life stress has been linked to changes in cardiovascular responses following laboratory stress, it has not been consistently found to sensitize individuals to laboratory stressors as theory would suggest. Findings regarding the direction of impact have been mixed. Matthews and colleagues (1997; 2001) found greater blood pressure reactivity to laboratory stressors among those with greater background life stress. In contrast, Boyce and Chesterman (1990) found that adolescents with a high number of life events demonstrated muted cardiovascular reactivity to several laboratory stressors. Cumulative life stress risk was also associated with muted reactivity and slower, less efficient blood pressure recovery following mental arithmetic (Evans, Kim, Ting, Tesher, & Shannis, 2007). Similarly, Lepore et al. (1997) found delayed recovery in those with greater background stress. Roy and colleagues (1998), on the other hand, found no relation between background life stress and cardiovascular reactivity in another study.

Differences in the sensitizing effects of background life stress exposure on laboratory stress responses may reflect differences in the operationalization of background life stress or may be moderated by other factors that confer stress vulnerability (Roy, et al., 1998). Response patterns may be task-dependent or dependent on the physiological response being measured. For example, Musante et al. (2000) found that youth who reported higher levels of background life stress showed smaller increases in blood pressure and heart rate to a car-driving task and larger increases in cardiac output following a social stressor interview than youth who reported low levels of background life stress. Inoculation effects and "cost of coping" were offered as explanations of these findings, respectively. Thus, it may be that chronic overactivity or underactivity of allostatic (or adaptive) systems which both can result from a history of high background life exposure may be manifest in increased sensitivity, heightened or decreased

activation, or decreased habituation upon exposure to new stressors (McEwen, 1998, 2004; McEwen & Wingfield, 2003).

The extent to which physiological responses to laboratory stress are associated with adverse health outcomes and disease (pathway b) has been well-studied (Chida & Hamer, 2008). Recent studies have supported that greater cardiovascular reactivity in the laboratory and poorer recovery have generally been associated with future blood pressure, hypertension, and subclinical disease (Boyce, et al., 1995; Carroll, Ginty, et al., 2012; Chatkoff, Maier, & Klein, 2010; Hamer & Malan, 2010; Low, Salomon, & Matthews, 2009; Manuck, 1994; Matthews, Salomon, Brady, & Allen, 2003; Schwartz, et al., 2003; Steptoe & Marmot, 2005; Treiber, et al., 2003). Cardiovascular reactivity has also been associated with self-reported health and physical disability (Phillips, 2011; Phillips, Der, Shipton, & Benzeval, 2011), with blunted reactivity associated with depression and worse health. Additionally, autonomic reactivity has been linked with internalizing and externalizing psychopathology (Boyce, et al., 2001; Kibler & Ma, 2004).

Pathways Among Background Life Stress, Physiological Response, and Health in FAP

While laboratory stress reactivity has not been examined as a mediator of the relation between life stress and health outcomes in FAP, there is theoretical support for the noted pathways. According to Chang (2011), "the role of stress may be particularly important in altering brain-gut interactions, resulting in the development and/or exacerbation of IBS symptoms" (p. 761). This author goes on to assert that a "conceptual pathophysiologic model for IBS" can include the relation of gastrointestinal symptoms in IBS with "central factors such as stressful or traumatic life events, the frequently reported co-morbidity with anxiety disorders, and peripheral factors such as gut inflammation, motility, and sensation" (p. 761). It

has been posited that the autonomic system, in combination with other components of the "emotional motor system" such as neuroendocrine and attentional systems, mediates the effects of psychological stressors on brain-gut interactions and gut functioning (Mayer & Collins, 2002; Mayer, et al., 2001). As such, central nervous system dysregulation has been described as "causative in FGID symptom onset and maintenance" (Levy, et al., 2006; Mönnikes, et al., 2001).

As previously described, empirical evidence supports the pathway from background life stress to symptom exacerbation and other health outcomes (pathway c') in FGIDs (e.g., Bennett, et al., 1998; Gwee, et al., 1999; Whitehead, et al., 1992). In addition, there has been much attention to a history of abuse and neglect particularly in individuals with IBS (Chitkara, van Tilburg, Blois-Martin, & Whitehead, 2008; Ross, 2005; Talley, Fett, Zinsmeister, & Melton, 1994; Videlock, et al., 2009). However, no published studies to date have examined the relation between background life stress and cardiovascular responses to laboratory stress in FAP, nor have any studies of FAP linked background life stress to other non-cardiovascular physiological responses (pathway b). Studies examining the relation of cardiovascular responses to health outcomes in FAP have focused primarily on pain-related outcomes such as increased pain sensitivity (lower pain tolerance) with increased cardiovascular reactivity (Caceres & Burns, 1997; Dufton, et al., 2008).

Childhood Background Life Stress

As noted previously, patterns of biobehavioral responding to stress are established in childhood (McEwen, 2003; Repetti, et al., 2002). Overall, early adversity is thought to be more predictive of adverse outcomes (Gunnar & Quevedo, 2007). It has been widely cited that the

more chronic and enduring the stressors, the more potential for damage (McEwen, 2004; Miller, Chen, & Zhou, 2007). The studies reviewed thus far have underscored the importance of somewhat recent background life stressors in an individual's response to future stressors, and greater recent background life stress has been associated with adverse health outcomes.

Based on prior research, individuals with more longstanding life stress (e.g., with high background life stress beginning in childhood) may develop adverse health outcomes later in life. High childhood background life stress may combine with patterns of reactivity and reflect the diathesis-stress model at play early in life. In addition, high childhood background life stress may be associated with greater allostatic load given the more longstanding history of responding to stressors. It would be expected that those with high background life stress both in childhood and young adulthood would have the highest risk of adverse health outcomes and the most dysregulated physiological responses in acute stress situations. As such, Heim et al. (2003) found that a history of childhood trauma predicted laboratory reactivity even when controlling for abuse experienced as an adult. In another study, Heim et al. (2002) showed that the interaction between childhood abuse history and the number of adulthood traumas was the overall best predictor of neuroendocrine reactivity levels such that a history of childhood abuse with additional trauma in adult was associated with the highest responses to stress. However, such an additive model has yet to be explored in FAP and with measures of cardiovascular response following laboratory stressors.

Rationale for the Current Study and Hypotheses

FAP is a common recurrent pain condition that has been associated with high levels of stress. The literature demonstrates a significant association between background life stress and a

host of adverse health outcomes, but the strength of this relation is most likely affected by other factors. One such factor is physiological reactivity to and recovery from acute stress. Physiological response might be implicated in two ways: as a moderator, consistent with the diathesis-stress model, or as a mediator, consistent with the framework of allostatic load. Studies of moderation have suggested a trait-like orientation to high or low reactivity and have shown that individuals with high levels of reactivity have worse health outcomes under conditions of high background life stress. However, although many studies (Chang, et al., 2008; Dorn, et al., 2003; Dufton, et al., 2008; Elsenbruch, et al., 2001; Jørgensen, Bønløkke, & Christensen, 1986; Mazurak, et al., 2012) have demonstrated higher reactivity and poorer recovery to laboratory stress among FAP compared with healthy controls, no studies have examined physiological responses in FAP and associated health outcomes as a function of background life stress.

Though the theoretical literature supports physiological reactivity as a potential mediator in the relation between background life stress and health outcomes, studies conducted to date have used cross-sectional designs in testing mediation effects. However, longitudinal data are needed to establish mediation (Cole & Maxwell, 2003; Maxwell & Cole, 2007). Nonetheless, cross-sectional data may be useful in an examination of the direct pathways between variables to provide a preliminary basis for future testing of indirect effects and mediation. However, even the direct pathways between the variables have not been examined in FAP. Each of these relations is important in providing clues to the potential role of cardiovascular response to acute stress. Many studies have linked background life stress to symptom outcomes in FAP. Few studies in FAP, however, have attempted to evaluate the pathway between background life stress and physiological reactivity. There is some support in the literature for the effect of physiological reactivity on adverse pain-related outcomes in FAP (Caceres & Burns, 1997;

Dufton, et al., 2008), but no studies to date have examined other physical and mental health outcomes.

Examination of the impact of physiological reactivity and recovery on health outcomes may be useful in understanding pathways of health risk and in understanding the interacting effects of psychosocial stressors and physiological reactivity to subsequent acute stressors on long-term health outcomes. As Clements and Turpin (2000) note, "a common approach has been the use of either life event questionnaires or interviews, alongside either the prospective or retrospective study of psychological well-being and health status, in clinical or high-risk groups" (p. 74). The present study employed such a research design in a sample of adolescents and young adults with and without a history of pediatric-onset FAP along with the measurement of physiological responses to laboratory stress tasks. Background life stress and both psychological and physical health outcomes were assessed via questionnaires. Among those with a history of childhood FAP, data on childhood family stress were also available. Cardiovascular responses (reactivity and recovery) were assessed via blood pressure measured in response to a social and a cognitive laboratory stressor.

The current study had two primary aims: 1) examine cardiovascular response to laboratory stress as a moderator of the relation between background life stress and health outcomes; and 2) examine direct pathways linking background life stress to health outcomes, background life stress to cardiovascular responses to laboratory stress, and cardiovascular responses to laboratory stress to health outcomes in childhood FAP patients at long-term follow-up. A secondary aim was to explore the role of childhood family stress as a potential moderator of these direct pathways in individuals with a history of childhood FAP.

The hypotheses for this study are as follows:

Hypothesis 1: Controlling for age, sex, and body mass index (BMI), cardiovascular responses (blood pressure reactivity and recovery) following laboratory stress tasks will moderate the relation between background life stress and health outcomes. For those with high reactivity to or diminished recovery from laboratory stress, the relation between background life stress and health outcomes will be stronger than for those with low reactivity to or greater recovery from laboratory stress. The moderating effect of cardiovascular responses in the relation between background life stress and health outcomes will be stronger for those with a history of childhood FAP than healthy controls, controlling for age, sex, and BMI.

Hypothesis 2: There will be significant relations among background life stress, cardiovascular responses to laboratory stress, and health outcomes. The relations will be stronger for participants with a history of childhood FAP compared with healthy controls.

Hypothesis 2a: Controlling for age, sex, and BMI, greater background life stress will be associated with greater negative health outcomes. This relation will be stronger for those with a history of childhood FAP than for healthy controls, controlling for age, sex, and BMI.

Hypothesis 2b: Controlling for age, sex, and BMI, greater background life stress will be associated with greater cardiovascular reactivity to and diminished recovery from laboratory stressors. This relation will be stronger for those with a history of childhood FAP than for healthy controls.

Hypothesis 2c: Controlling for age, sex, and BMI, greater cardiovascular reactivity to and diminished recovery from laboratory stress will be significantly associated with greater negative health outcomes. This relation will be stronger for those with a history of childhood FAP than healthy controls.

Hypothesis 3: For those with a history of childhood FAP and high cardiovascular reactivity to or slow recovery from laboratory stress, the relation between recent background life stress and health outcomes will be stronger for those with high childhood family stress than low childhood family stress, controlling for age, sex, and BMI. For those with low cardiovascular reactivity to and better recovery from laboratory stress, lower health outcomes is expected regardless of childhood family life stress and background life stress.

CHAPTER II

METHOD

Overview

This study reports on data that were collected as part of a comprehensive prospective study evaluating health outcomes of pediatric-onset FAP. Other aspects of the evaluation are presented elsewhere (Bruehl, Dengler-Crish, Smith, & Walker, 2010; Walker, et al., 2010; Walker, Sherman, Bruehl, Garber, & Smith, 2012). Participants in the current study were adolescents and young adults with a history of childhood FAP and healthy controls who completed both the laboratory portion of the study and the measure of background life stress administered at follow-up. For participants under age 18, a parent also participated at follow-up.

Participants

Childhood Functional Abdominal Pain (FAP) Group

Participants for the FAP group were recruited for this study from a database of approximately 850 consecutive new patients referred to the pediatric gastroenterology clinic at Vanderbilt for evaluation of abdominal pain of at least three months' duration. Participants were 8 to 16 years of age when they were enrolled in studies conducted by Walker and colleagues between 1993 and 2004 (Walker, Baber, Garber, & Smith, 2008; Walker, et al., 2001; Walker, Smith, Garber, & Claar, 2005). The parent who accompanied the child to the clinic visit also participated in baseline assessment. For these original studies, eligibility criteria included

abdominal pain of at least 3 months duration, no chronic illness or disability, and no diagnosis from the referring physician of an organic disease for abdominal pain. Consent/assent for participation in the baseline assessment and for contacting about future studies was obtained.

Several months after enrollment in the initial study, medical records were reviewed for results of the medical evaluation. Patients whose medical evaluation at Vanderbilt yielded evidence of significant organic disease (e.g., ulcerative colitis) were excluded from the present study. For the present study, eligibility criteria included: no evidence of significant organic disease in the pediatric gastroenterology evaluation of FAP, 12 years of age or older at the time of follow-up, at least 4 years elapsed since initial study enrollment, and no subsequent gastrointestinal or other major chronic disease (e.g., multiple sclerosis, lupus) by self-report.

Healthy Controls

The healthy control group was drawn from a database of over 350 children recruited from community schools who had participated in healthy control groups for previous studies (Walker, et al., 2008; Walker, et al., 2001; Walker, et al., 2005; Walker, Smith, Garber, & Van Slyke, 1997). These youth were between the ages of 8 and 16 years at the time of study enrollment. At baseline, eligibility included no chronic illness and no abdominal pain in the month preceding initial study participation. For the present study, eligibility included: no abdominal pain in the month preceding enrollment in the original study, age 12 years or older at follow-up, at least 4 years elapsed since initial study enrollment, and no gastrointestinal or other major chronic disease (e.g., multiple sclerosis, lupus) based on self-report at follow-up.

Measures and Stimuli

Self-report Measures

Demographic factors. Participants or parents (for participants under age 18) indicated participant age, sex, and race/ethnicity.

Socioeconomic status. The Hollingshead Index of Socioeconomic Status is based on occupation and level of education. Scores can range from 8 (unskilled laborer) to 69 (professional). Education was rated on a scale from "1" (less than seventh grade) to "7" (graduate degree). The scale value for occupation is multiplied by a weight of five, and the scale value for education was multiplied by a weight of three; these numbers then were summed for a total score for single adults. For married adults, the Hollingshead score was the average of the scores of each spouse. For adolescents, the Hollingshead score was based on the occupation and education of the parent(s) with whom the child lived.

Childhood family stress. The Family Inventory of Life Events (FILE; McCubbin & Patterson, 1987) is a parent-report measure of the number of family life events experienced in the year preceding initial baseline participation. A summary score was computed to determine the total number of life events. Only parents of FAP participants completed the FILE at the initial baseline visit. Alpha reliability was .76.

Self-reported background life stress. A modified version of the FILE for self-report by adolescents and young adults was used and comprised the Life Events Checklist (LEC). The LEC assessed the presence or absence of major life events in the last year. A summary score was computed to determine the total number of life events. Alpha reliability was .81.

Self-reported abdominal pain symptoms. The Rome III Diagnostic Questionnaire for Functional Gastrointestinal Disorders (FGID; Drossman, 2006) assesses for the current Rome III diagnostic symptom criteria for functional gastrointestinal disorders (FGIDs) established by the Rome Foundation Board. This 24-item measure assessed symptom criteria for FGIDs associated with abdominal pain, including irritable bowel syndrome, functional dyspepsia, abdominal migraine, and functional abdominal pain. Participants' responses were scored according to the pediatric Rome criteria (for participants under 18 years of age) or the adult Rome criteria (for participants 18 years and older).

Self-reported health. Participants completed the 36-item Short Form Health Survey (SF-36; Ware & Sherbourne, 1992) which assesses eight domains of health perception. For this study, the 5-item general health perceptions scale (including current health, health outlook, and resistance to illness) and the 5-item general mental health scale (including depression, anxiety, behavioral-emotional control, & general positive affect) were used. Raw scores for each subscale were calculated. Item scores were coded, summed, and transformed to a scale from 0 (worst possible health state measured by the questionnaire) to 100 (best possible health state). Alpha reliabilities for the general and mental health scales were .82 and .74, respectively.

Self-reported somatic symptoms. Participants completed the Children's Somatization Inventory (CSI; Garber, Walker, & Zeman, 1991; Walker, et al., 1991). Of note, while the title includes the word "child" the measure does not ask child-specific items and therefore was used with the adolescent and young adult participants. The CSI assesses perceived severity of 9 gastrointestinal (GI) symptoms (e.g., abdominal pain, nausea, constipation) and 26 non-GI somatic symptoms (e.g., dizziness, headaches). In this study, non-GI symptoms were of interest. For each item, participants rate "How much were you bothered by (*symptom*)?" during the past

two weeks on a 5-point scale ranging from "not at all" (0) to "a whole lot" (4). The non-GI subscale score was computed by summing the scores across items. Alpha reliability for the non-GI symptom subscale was .82.

Self-reported functional disability. The Functional Disability Inventory (FDI; Claar & Walker, 2006; Walker & Greene, 1991a) assesses self-reported difficulty in physical and psychosocial functioning due to physical health during the past 2 weeks. Responses to each of the 15 items are scored on a 5-point scale, ranging from (0) no trouble to (4) impossible, and are summed to yield a total score that can range from 0 to 60. Alpha reliability was .85.

Laboratory Stress Tasks

Social Competence Interview (SCI). The Social Competence (SCI; Ewart, Jorgensen, Suchday, Chen, & Matthews, 2002; Ewart & Kolodner, 1991) is a semi-structured interview developed to induce emotional stress and cardiovascular arousal in the laboratory by having participants discuss details of stressful life situations. Participants were asked to select from a list of common stressors the problem that causes them the most recurring stress in the past few months (work, school, friend, neighborhood, family, and money). With a set of questions asked by the interviewer, the participants explained why this problem has been stressful and reconstructed a specific problem situation by describing in detail where it occurred and what happened. This re-experiencing portion constituted in the first portion of the interview (the hot or active phase). In the second portion of the interview, participants were participants were asked how they wish the problem could be resolved, what they might do to achieve this outcome, how confident they are that they could take the needed actions, and what consequences might ensue (cool phase). The SCI in total was designed to last between 8 and 14 minutes.

Serial Subtraction (SS). Participants completed a mental arithmetic laboratory stress task which was a serial subtraction task (Jorgensen & Houston, 1986). Participants were instructed to begin with the number 400 and serially subtract by the number 7 for two minutes. Participants were instructed to make a subtraction out loud at least every 3 seconds, and to make the subject aware of this rate, a recording of beeps occurring at 3-second intervals were played. When an incorrect answer was given, participants were told, "That was incorrect. Start over at 400." To increase the stressfulness of the task, the experimenter told the participant to try to keep up with the beeps when they fell behind. For participants who were unable to perform this task, the experimenter instructed those participants to subtract from 100 by the number 7.

Cardiovascular Response

Blood pressure (BP). Blood pressure (BP) at baseline and during the laboratory stressors was assessed every two minutes using a Dinamap Compact-T automated oscillometric BP monitor (Dinamap; Johnson & Johnson, Inc) with the cuff placed on the bicep of the dominant arm. The parameters assessed via the Dinamap included systolic blood pressure (SBP) and diastolic blood pressure (DBP). Baseline included four measurement points. A variable number of measurements were recorded during the SCI depending on the length of the interview. This first portion of the SCI (hot or active phase) reliably produces increases in sympathetic arousal (C. Ewart, personal communication). In the second portion of the SCI (cool phase), participants were asked about their coping goals including how they wished the stressor or problem to be resolved. This portion of the SCI is associated with a return to baseline indices of autonomic arousal (C. Ewart, personal communication). Measurements taken during the SCI hot phase and cool phase were averaged separately. The post-SCI recovery phase included four BP

measurements. During the 2-minute mental arithmetic, two measurements were taken, one at the beginning and one two minutes later. The readings observed within each epoch were averaged to yield a single estimate for each epoch.

Procedure

Recruitment

At the time of the original baseline assessment, parents and youth gave consent and assent, respectively, to be contacted regarding future studies. Newsletters were sent to families of FAP and healthy control participants periodically to maintain contact and update addresses. Participants were contacted 4 to 16 years later regarding participation in the present follow-up study. Participants were recruited to participate in a structured telephone interview for the follow-up study. For participants under age 18, both the parent and child were interviewed about the child's symptoms. All participants in the follow-up study were invited to the Vanderbilt Pediatric Clinical Research Center to participate in a laboratory portion of the study.

The FAP patient database was reviewed to identify participants who met eligibility criteria for age and follow-up interval (n = 760). Of those who met criteria, 261 (34%) could not be reached by telephone, 60 (8%) declined to participate, and 40 (5%) did not keep their appointment or could not be scheduled during the study period. Three were excluded because of self-reported onset of chronic disease during the follow-up interval (inflammatory bowel disease, celiac disease, multiple sclerosis). Of the 391 FAP participants who completed the health interview portion of the follow-up study, 240 (62%) participated in the laboratory portion of the study and completed the measure of background life stress. For participants under age 18 at

follow-up (n = 51), the parent who participated at baseline also completed an interview at follow-up.

The healthy control group database (n = 343) was also reviewed to identify potential participants who met eligibility criteria. Of these healthy controls, 110 (32%) could not be reached by telephone, 23 (7%) declined to participate, and 23 (7%) did not keep their appointment for the study or could not be scheduled. Of the healthy control group, 136 individuals participated in the laboratory portion of the study and completed the measure of background life stress. For participants under age 18 at follow-up (n = 41), a parent also participated at follow-up.

Participants in the FU assessment did not differ significantly from non-participants on sex, age, or baseline levels of abdominal pain.

Protocol

All procedures were approved by the Vanderbilt Institutional Review Board. In the initial baseline study, parents of FAP participants completed the FILE. For the current study, after providing informed consent, participants were interviewed about their health over the phone. For participants under age 18, a parent also was interviewed about their child's symptoms. The following measures are completed over the phone: Demographics, SF-36, FDI, CSI, and Rome III Questionnaire. Interviewers were unaware of participants' group status. All participants had the option to participate in a laboratory portion of the study to take part in the psychophysiological assessment protocol designed to evaluate stress responsiveness.

Consent/assent was obtained separately for follow-up interviews and laboratory testing. Standard instructions were provided for all participants prior to beginning the protocol.

Experimenters were unaware of participants' group status. Participants' height and weight were assessed. The blood pressure cuff was placed, and BP was recorded every 2 minutes. Participants were then instructed to sit quietly and view a slideshow for 6 minutes while baseline physiological measurements were obtained. After this baseline period, participants were exposed to the social laboratory stressor, the SCI, during which physiological reactions were measured. Participants were then instructed to sit quietly and view a second slideshow while post-SCI recovery physiological measurements were obtained for 6 minutes. The 2-minute SS task was then administered, with BP taken at the beginning and end of the 2-minute task. At the end of the laboratory session, participants were debriefed. Participants remained seated upright in a comfortable chair throughout all laboratory procedures.

Participants were then asked at the end of the laboratory session to complete a set of questionnaires on the computer via Survey Monkey which included the LEC. As the LEC is the primary independent variable of interest in this study, only participants who completed the Survey Monkey portion of the study were included in analyses.

CHAPTER IV

RESULTS

Data Analysis Overview

Analyses used PASW statistical package (version 18). Data analyses were conducted in several stages.

Sample Characteristics

Data Analytic Strategy

First, descriptive statistics (i.e., central tendency, variability, skewness, kurtosis) were examined for all study variable distributions, and any multivariate outliers were identified and removed. Variables not meeting the assumptions of normality or variables without having adequate variance and distribution to allow for correlation and regression analyses were log transformed.

Cleaning of the physiological data also underwent this process where both within and between subjects outliers by group and within each of the epochs (baseline, SCI, Recovery, and SS) were removed. Cardiovascular reactivity was represented by residualized change scores which were calculated by regressing BP levels during the SCI and SS stressor tasks on baseline BP, conducted separately for systolic and diastolic BP. Post-SCI recovery was represented by residualized change scores which were calculated by regressing BP levels during the recovery phase on baseline BP. Bivariate correlations among demographic variables (i.e., age, sex, BMI),

background life stress, blood pressure at each epoch, reactivity scores, and health outcomes scores were examined. Due to missing data, n's for analyses ranged from 347 to 366.

Results of Descriptive Analyses

Sample characteristics by group are presented in Table 1. Of 240 previously identified FAP patients who participated in the current follow-up study, 1 participant was excluded from further analyses due to extreme value for BMI (over 60). Of the remaining 239 in the childhood FAP group, 140 participants (58.6%) did not meet criteria for an FGID at follow-up while 99 (41.4%) participants did meet criteria for an FGID associated with abdominal pain at follow-up. Of the healthy control group, 9 (7.1%) met criteria for a FGID at follow-up; they were excluded from further analyses, leaving a healthy control sample of 127 for data analysis.

Means and standard deviations for demographic variables are presented in Table 1. The proportion of females differed significantly by group and was higher in the childhood FAP group, X^2 (1, N = 366) = 5.09, p = .01. The majority of participants in both groups were Caucasian. The follow-up interval ranged from 4 to 16 years (M = 8.02; SD = 3.02) and was slightly longer for the FAP group compared to the healthy control group. Age at baseline participation ranged from 8 to 18 (M = 11.44; SD = 2.41). Age at follow-up ranged from 12 to 31 years (M = 19.50; SD = 3.36). At follow-up, the healthy control group was slightly younger than FAP group, X^2 (1, N = 366) = -6.15, p < .001. Groups did not differ in socioeconomic status at follow-up. Mean BMI was significantly lower for healthy controls compared to FAP, X^2 (1, N = 366) = -3.82, p < .001.

Descriptive statistics for independent and dependent variables are also presented in Table 1. FAP reported significantly higher levels of background life stress than healthy controls, t(364)

= -2.46, $p < .05$. Compared to healthy controls, participants with a history of childhood FAP self-reported significantly poorer general health, $t(364) = 6.34$, $p < .001$, and mental health, $t(364) = 3.20$, $p < .01$. FAP also reported greater functional disability, $t(364) = -4.99$, $p < .01$, and higher somatic symptoms, $t(364) = -6.42$, $p < .001$. FAP and healthy controls did not differ in blood pressure at baseline, during the SCI, during recovery, or during SS. Mean BP levels increased for all participants in response to the laboratory stressors, and both groups returned to baseline BP levels during the post-SCI recovery phase.

Table 1. Descriptive Statistics.

Variables	Participant Group		*p*-value
	FAP (n = 239)	Healthy Controls (n = 127)	
% FAP Positive at Follow-up	41.4%	7.1%*	--
Sex (% Female)	65%	53%	.02
Race and Ethnicity (% Caucasian)	89%	95%	n.s.
Age at Baseline (years)	11.73 (2.53)	10.89 (2.08)	.001
Follow-up Interval (years)	8.47 (3.29)	7.17 (2.20)	<.001
Age at Follow-up (years)	20.19 (3.48)	18.18 (2.68)	<.001
Socioeconomic status at Follow-up	39.13 (11.62)	37.23 (11.78)	n.s.
Body Mass Index	26.61 (7.58)	24.08 (5.03)	<.001
Background Life Stress	8.43 (5.70)	6.98 (4.70)	.01
Childhood Family Stress †	6.03 (4.96)	--	--
SF-36 General Health	65.90 (22.82)	80.17 (15.20)	<.001
SF-36 Mental Health	75.95 (15.10)	81.04 (13.29)	.001
Somatic Symptoms	14.17 (10.83)	7.51 (5.94)	<.001
Functional Disability	4.30 (5.85)	1.58 (2.65)	<.001
Baseline SBP	112.05 (10.67)	110.48 (9.58)	n.s.
Baseline DBP	61.67 (7.30)	60.32 (6.17)	n.s.
SCI Active SBP	124.01 (13.51)	124.08 (12.11)	n.s.
SCI Active DBP	72.11 (8.98)	73.04 (8.20)	n.s.
Recovery SBP	112.04 (10.82)	111.21 (9.37)	n.s.
Recovery DBP	61.83 (7.32)	61.28 (6.82)	n.s.
SS SBP	122.70 (14.31)	124.02 (13.68)	n.s.
SS DBP	70.85 (8.54)	72.02 (8.30)	n.s.

Notes: Data are presented as means ± SD.
*Healthy controls who were FAP-Positive at Follow-up were excluded from further analyses.
†Parents of healthy control participants did not complete the FILE at baseline.
FAP = Functional Abdominal Pain. SBP = Systolic Blood Pressure. DBP = Diastolic Blood Pressure. SCI = Social Competence Interview. SS = Serial Subtraction.

Cardiovascular reactivity by group is summarized is Table 2. Overall, the healthy control group had positive residualized scores indicating greater BP responses during each epoch than would be predicted based on their baseline BP. Those with a history of childhood FAP, on the other hand, had negative residualized scores during each epoch, indicating BP responses that were lower than expected based on baseline BP throughout the task. For SCI DBP, healthy controls demonstrated higher residualized scores than FAP, $t(349) = 3.30$, $p < .01$. Similarly, for SS SBP and DBP, healthy controls demonstrated higher residualized scores than those with a history of childhood FAP, $t(348) = 2.69$, $p < .01$, and $t(348) = 3.36$, $p = .001$, respectively. These findings indicate that for both stressors, greater BP reactivity was observed in the healthy controls than in the childhood FAP participants. SCI SBP reactivity did not differ significantly between groups, nor did post-SCI recovery. Within group paired sample t-tests revealed no differences in BP reactivity between the SCI and SS stress tasks for childhood FAP or healthy controls.

Table 2. Residualized Change Scores for Blood Pressure by Group.

Variables	Participant Group		p-value
	FAP (n = 239)	Healthy controls (n = 127)	
SCI SBP Reactivity	-.50 (7.86)	.94 (8.75)	n.s.
SCI DBP Reactivity	-.74 (5.63)	1.38 (5.91)	< .01
Post-SCI SBP Recovery	-.12 (4.39)	.22 (4.88)	n.s.
Post-SCI DBP Recovery	-.22 (3.08)	.42 (3.55)	n.s.
SS SBP Reactivity	-1.00 (9.38)	1.85 (9.64)	< .01
SS DBP Reactivity	-.81 (6.10)	1.50 (6.19)	< .01

* p < .05, ** p < .01, *** p < .001
Notes: Data are presented as means ± SD.
FAP = Functional Abdominal Pain. SBP = Systolic Blood Pressure. DBP = Diastolic Blood Pressure. SCI = Social Competence Interview. SS = Serial Subtraction.

Bivariate correlations of all variables are presented in Table 3. Background life stress was significantly and positively correlated with childhood family stress (r = .28, $p < .001$). Background life stress was also significantly greater amongst females (r = -.20, $p < .001$) and was significantly and positively correlated with age (r = .12, $p < .05$). For the overall sample, correlations of background life stress and health outcomes (general and mental health, somatic symptoms, and functional disability) ranged from -0.2 to 0.4 (see Table 3; all *p*'s < .01). Background life stress was also significantly and inversely correlated with SBP reactivity to the SS task but not baseline blood pressure or other blood pressure reactivity to stress tasks.

Table 3. Bivariate Correlations.

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1. Background life stress	—																	
2. Childhood family stress	.28***	—																
3. Sex	-.20***	-.18*	—															
4. Age	.13*	.09	-.05	—														
5. BMI	.01	.06	-.04	.30***	—													
6. SES	-.13	.2	.03	-.17**	-.18**	—												
7. General health	-.22***	-.12	.27***	-.18**	-.25***	.02	—											
8. Mental health	-.37***	-.09	.24***	-.06	-.06	.04	.47***	—										
9. Somatic symptoms	.29**	.22**	-.19**	.17**	.16**	-.02	-.51**	-.49**	—									
10. Functional disability	.26***	.22***	-.19***	.17**	.16**	-.02	-.56***	-.50***	.74***	—								
11. Baseline SBP	-.09	.03	.44***	.10	.28***	-.12*	.06	.08	-.06	-.01	—							
12. Baseline DBP	.04	.11	-.003	.34***	.04	-.09	-.07	-.10	.06	.06	.44***	—						
13. SCI SBP reactivity	-.01	-.17*	.17**	-.05	-.21**	.01	.13*	.00	-.07	-.10	.00	.05	—					
14. SCI DBP reactivity	-.04	-.14	.07	-.13*	-.17	-.02	.10	.00	-.11*	-.11*	.10	.00	.58**	—				
15. SBP recovery	.06	-.01	.13*	.06	.04	.02	.03	.00	.11*	.05	.00	.09	.47**	.17**	—			
16. DBP recovery	.01	.00	-.01	.06	-.15**	-.12	-.04	00	.05	-.01	-.08	.00	.20**	.30**	.41**	—		
17. SS SBP reactivity	-.15**	-.16*	.29**	-.01	-.14**	.06	.15**	.05	-.16**	-.12*	.00	.03	.47**	.30**	.29**	.13*	—	
16. SS DBP reactivity	-.09	.05	.21**	-.05	-.15**	.04	.12*	.11*	-.17**	-.15**	.08	.00	.37**	.44**	.16**	.32**	.62**	—

* p < .05, ** p < .01, *** p < .001

Notes: BMI = Body Mass Index. SES = Socioeconomic Status. SBP = Systolic Blood Pressure. DBP = Diastolic Blood Pressure. SCI = Social Competence Interview. SS = Serial Subtraction

Hypothesis Testing

Data Analytic Strategy

The analytic procedures used to address each hypothesis are detailed below. For all analyses, continuous control and dependent variables were centered on their means.

To test Hypothesis 1 that cardiovascular stress responses moderate the relation between background life stress and health outcomes in those with and without a history of childhood FAP, a series of linear multiple regressions were conducted. Separate regressions were run for each of the health outcomes that were the dependent variables of interest: general and mental health, somatic symptoms, and functional disability. Separate regression equations were also run for cardiovascular reactivity and recovery, for systolic and diastolic BP, and for each laboratory stress task. Control variables (age, sex, and BMI) were entered in the first step. Predictor variables of group, background life stress, and cardiovascular stress responses were entered in the second step. Terms representing the two-way interactions among group, background life stress, and cardiovascular stress responses were entered in the third step. The three-way interaction of background life stress, cardiovascular reactivity and recovery, and group was entered in the fourth step.

To test Hypothesis 2 that there will be significant relations among background life stress, cardiovascular responses to laboratory stress, and health outcomes that differ between those with and without a history of childhood FAP, a series of hierarchal multiple regression analyses were conducted:

To examine the relation of background life stress to the various health outcomes of interest in those with and without a history of childhood FAP, hierarchical multiple regressions

included control variables (age, sex, and BMI) entered in the first step. Main effects of background life stress and group were entered in the second step. In the third step, the two-way interactions of background life stress and group were entered. Regression models were run separately for each of the dependent variables.

Hierarchical multiple regression was also used to examine the impact of background life stress on cardiovascular stress reactivity and recovery in those with and without a history of childhood FAP. Analyses included age, sex, and BMI as control variables in the first step, main effects of background life stress and group entered in the second step, and the two-way interactions of background life stress and group entered in the third step. Separate regression models were run for SBP and DBP during the SCI and SS tasks, and post-SCI recovery SBP and DBP analyses were also run separately. The impact of background life stress on baseline BP was also examined.

Hierarchical multiple regression was used to examine the impact of cardiovascular reactivity during each laboratory stress task and post-SCI recovery on health outcomes in those with and without a history of childhood FAP. Separate regression models were run for SBP and DBP during the SCI and SS tasks as well as post-SCI recovery. Control variables were age, sex, and BMI. In the second step, main effects of cardiovascular responses and group were entered, and the two-way interactions of group and cardiovascular response were entered in the third step.

To examine Hypothesis 3 that, among those with a history of childhood FAP, childhood family stress will be moderate the relations of background life stress and cardiovascular responses on health outcomes, a series of hierarchical multiple regression analyses were conducted. Separate regression equations were run for each of the health outcomes that were the dependent variables of interest: general and mental health, somatic symptoms, and functional

disability. Control variables (age, sex, BMI) were entered in the first step. Background life stress, childhood family stress, and cardiovascular responses were entered in the second step. Terms representing the two-way interactions of background life stress with childhood family stress, background life stress, cardiovascular responses, and childhood family stress were entered in the third step. The three-way interaction of background life stress, childhood family stress, and cardiovascular responses was entered in the fourth step.

Cardiovascular Responses as Moderators of the Relation Between Background Life Stress and Health Outcomes

Controlling for age, sex, and BMI, the interaction of background life stress with cardiovascular responses were not significantly related to any of the four health outcomes (see Tables 4-9). There was a significant three-way interaction among background life stress, SBP reactivity to the SCI task, and group on perceived general health ($\beta = 0.17$, $p = .03$) (see Table 4). Regression lines for childhood FAP and healthy controls with high (+1 SD) and low (-1 SD) levels of SCI SBP reactivity at high (+1 SD) and low (-1 SD) levels of background life stress were plotted to examine the nature of the interaction effect on perceived general health (Figure 3). For those with a history of childhood FAP with high SBP reactivity to the SCI, higher background life stress is associated with poorer perceived general health. For those with a history of childhood FAP with low SBP reactivity to the SCI, increased background life stress is not associated with poorer perceived general health. Among healthy controls, higher background life stress is associated with poorer perceived general health, but only among those with low SBP reactivity to the SCI.

Table 4. Interaction of Background Life Stress, SCI Systolic Blood Pressure Reactivity, and Group on Health Outcomes.

Predictor variable	Model 1: Perceived General Health [a]	Model 2: Perceived Mental Health [a]	Model 3: Somatic Symptoms	Model 4: Functional Disability
Step 1: Control variables				
Age	.09	.01	.11*	.11*
	(1.70)	(.09)	(2.07)	(2.01)
Sex	-.22***	-.23***	-.23***	-.19***
	(-4.28)	(-4.30)	(-4.42)	(-3.71)
BMI	.11*	.05	.09	.13*
	(2.01)	(.86)	(1.65)	(2.39)
Step 2: Predictor variables				
Group	.22***	.09	.21***	.24***
	(4.27)	(1.63)	(3.99)	(4.55)
Background life stress	.17**	.25***	.22***	.18**
	(3.23)	(4.85)	(4.38)	(3.51)
SCI SBP reactivity	-.003	.06	-.01	-.05
	(-.06)	(1.07)	(-.12)	(-.89)
Step 3: Primary Two-Way Interactions				
Background life stress X Reactivity	-.02	.07	.03	.02
	(-.36)	(1.30)	(.51)	(.38)
Background life stress X Group	-.05	-.02	.06	.10
	(-.54)	(-.28)	(.76)	(1.23)
Group X SCI SBP Reactivity	.04	.09	.01	.04
	(.47)	(1.05)	(.17)	(.48)
Step 4: Three-Way Interaction				
Background life stress X SCI SBP Reactivity X Group	.17*	.04	.07	.06
	(2.12)	(.46)	(.82)	(.71)

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
[a]Variables were log transformed; higher values represent poorer health.
* p < .05, ** p < .01, *** p < .001.
BMI = Body Mass Index. SCI = Social Competence Interview. SBP = Systolic Blood Pressure.

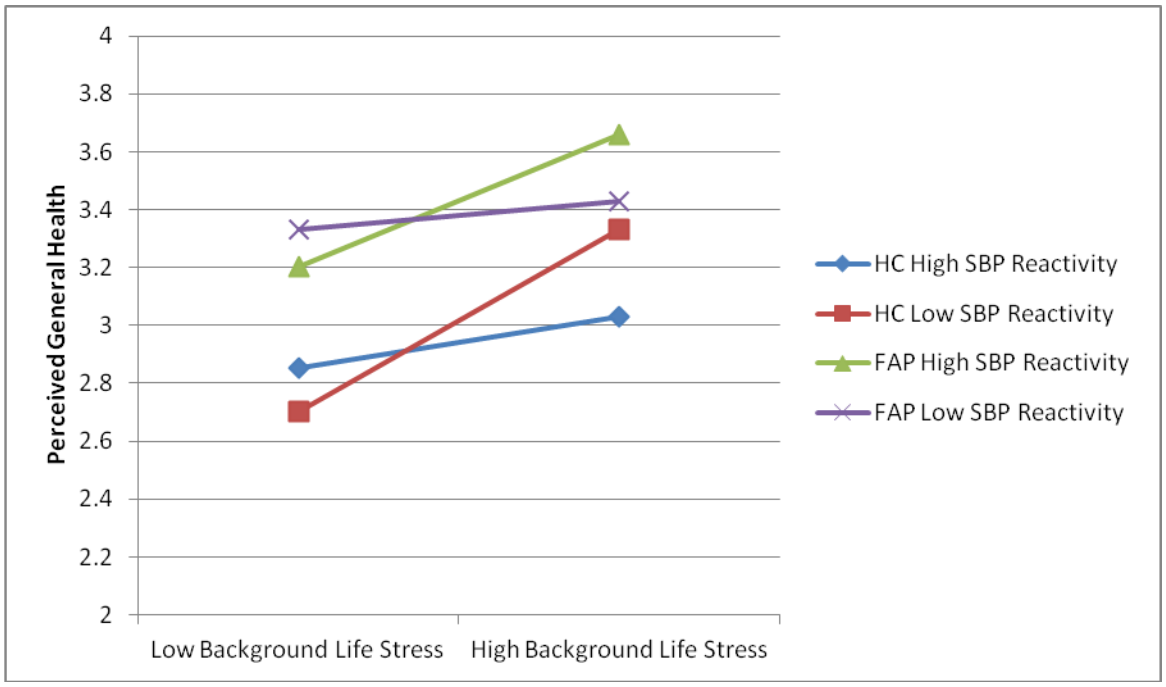


Figure 3. Regression lines showing predicted levels of perceived general health for childhood FAP and healthy control participants with low (-1 SD) and high (+1 SD) SBP reactivity at low (-1 SD) and high (+1 SD) levels of background life stress, controlling for age, sex, and BMI.

Table 5. Interaction of Background Life Stress, SCI Diastolic Blood Pressure Reactivity, and Group on Health Outcomes.

Predictor variable	Model 1: Perceived General Health [a]	Model 2: Perceived Mental Health [a]	Model 3: Somatic Symptoms	Model 4: Functional Disability
Step 1: Control variables				
Age	.09	.01	.11*	.11*
	(1.70)	(.09)	(2.07)	(2.01)
Sex	-.22***	-.23***	-.23***	-.19***
	(-4.28)	(-4.30)	(-4.42)	(-3.71)
BMI	.11*	.05	.09	.13*
	(2.01)	(.86)	(1.65)	(2.39)
Step 2: Predictor variables				
Group	.23***	.10	.20***	.24***
	(4.34)	(1.82)	(3.90)	(4.50)
Background life stress	.17**	.26***	.22***	.18**
	(3.23)	(4.91)	(4.38)	(3.48)
SCI DBP reactivity	.05	.10	-.02	-.02
	(.89)	(1.82)	(-.48)	(-.41)
Step 3: Primary Interactions				
Background life stress X	-.04	.003	-.01	.01
Reactivity	(-.74)	(.07)	(-.21)	(.17)
Step 4: Secondary Interactions				
Background life stress X	-.05	-.03	.06	.10
Group	(-.55)	(-.38)	(.69)	(1.25)
Group X Reactivity	-.07	.09	.06	.12
	(-.87)	(1.07)	(.78)	(1.39)
Step 5: Three-Way Interaction				
Background life stress X	.06	.05	.06	-.01
Reactivity X Group	(.80)	(.59)	(.78)	(-.16)

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
[a]Variables were log transformed; higher values represent poorer health.
* $p < .05$, ** $p < .01$, *** $p < .001$.
BMI = Body Mass Index. SCI = Social Competence Interview. DBP = Diastolic Blood Pressure.

Table 6. Interaction of Background Life Stress, SS Systolic Blood Pressure Reactivity, and Group on Health Outcomes.

Predictor variable	Model 1: Perceived General Health [a]	Model 2: Perceived Mental Health [a]	Model 3: Somatic Symptoms	Model 4: Functional Disability
Step 1: Control variables				
Age	.08	.003	.11	.11*
	(1.44)	(.05)	(1.93)	(1.99)
Sex	-.23***	-.22***	-.23***	-.19***
	(-4.38)	(-4.28)	(-4.43)	(-3.63)
BMI	.10	.05	.09	.13*
	(1.88)	(.86)	(1.56)	(2.34)
Step 2: Predictor variables				
Group	. 23***	.09	.20***	.23***
	(4.43)	(1.73)	(3.92)	(4.40)
Background life stress	.17**	.26***	.22***	.17**
	(3.24)	(4.97)	(4.33)	(3.30)
SS SBP Reactivity	.01	.08	-.07	-.09
	(.24)	(1.47)	(-1.41)	(-1.64)
Step 3: Primary Interactions				
Background life stress X Reactivity	-.03	-.001	-.04	-.02
	(-.55)	(-0.1)	(-.84)	(-.31)
Step 4: Secondary Interactions				
Background life stress X Group	-.06	-.05	.04	.10
	(-.70)	(-.55)	(.52)	(1.20)
Group X Reactivity	.13	-.06	.14	.11
	(1.50)	(-.64)	(1.61)	(1.30)
Step 5: Three-Way Interaction				
Background life stress X Reactivity X Group	.05	-.07	.01	-.01
	(.60)	(-.84)	(.09)	(-.12)

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
[a]Variables were log transformed; higher values represent poorer health.
* $p < .05$, ** $p < .01$, *** $p < .001$.
BMI = Body Mass Index. SS = Serial Subtraction. SBP = Systolic Blood Pressure.

Table 7. Interaction of Background Life Stress, SS Diastolic Blood Pressure Reactivity, and Group on Health Outcomes.

Predictor variable	Model 1: Perceived General Health [a]	Model 2: Perceived Mental Health [a]	Model 3: Somatic Symptoms	Model 4: Functional Disability
Step 1: Control variables				
Age	.08	.003	.11	.11*
	(1.44)	(.05)	(1.93)	(1.99)
Sex	-.23***	-.22***	-.23***	-.19***
	(-4.38)	(-4.28)	(-4.43)	(-3.63)
BMI	.10	.05	.09	.13*
	(1.88)	(.86)	(1.56)	(2.34)
Step 2: Predictor variables				
Group	.24***	.08	.20***	.22***
	(4.48)	(1.56)	(3.90)	(4.27)
Background life stress	.17**	.25***	.22***	.17***
	(3.25)	(4.86)	(4.32)	(3.36)
SS DBP Reactivity	.04	.00	-.05	-.11*
	(.67)	(-.01)	(-1.04)	(-2.09)
Step 3: Primary Interactions				
Background life stress X	.04	-.01	-.05	.05
Reactivity	(.77)	(-.12)	(-1.04)	(.96)
Step 4: Secondary Interactions				
Background life stress X	-.04	-.05	.03	.13
Group	(-.51)	(-.62)	(.40)	(1.56)
Group X Reactivity	-.02	-.14	.03	.11
	(-.18)	(-1.65)	(.35)	(1.27)
Step 5: Three-Way Interaction				
Background life stress X	-.08	.02	-.09	-.01
Reactivity X Group	(-.93)	(.22)	(-1.08)	(-.07)

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
[a]Variables were log transformed; higher values represent poorer health.
* $p < .05$, ** $p < .01$, *** $p < .001$.
BMI = Body Mass Index. SS = Serial Subtraction. DBP = Diastolic Blood Pressure.

Table 8. Interaction of Background Life Stress, Systolic Blood Pressure Recovery, and Group on Health Outcomes.

Predictor variable	Model 1: Perceived General Health [a]	Model 2: Perceived Mental Health [a]	Model 3: Somatic Symptoms	Model 4: Functional Disability
Step 1: Control variables				
Age	.08	-.01	.09	.10
	(1.39)	(-.09)	(1.73)	(1.50)
Sex	-.23***	-.23***	-.24***	-.20***
	(-4.47)	(-4.39)	(-4.68)	(-3.85)
BMI	.10	.05	.09	.13*
	(1.88)	(.93)	(1.62)	(2.35)
Step 2: Predictor variables				
Group	.23***	.09	.22***	.24***
	(4.42)	(1.66)	(4.19)	(4.64)
Background life stress	.17**	.26***	.22**	.18**
	(3.39)	(4.99)	(4.43)	(3.50)
Post-SCI SBP Recovery	-.07	.01	.07	.02
	(1.48)	(.21)	(1.46)	(.39)
Step 3: Primary Interactions				
Background life stress X Recovery	.003	.07	.04	-.01
	(.06)	(1.46)	(.85)	(-.24)
Step 4: Secondary Interactions				
Background life stress X Group	-.05	-.02	.05	.10
	(-.62)	(-.27)	(.66)	(1.24)
Group X Recovery	.11	-.04	.08	.08
	(1.35)	(-.52)	(1.02)	(1.03)
Step 5: Three-Way Interaction				
Background life stress X Recovery X Group	.11	-.11	-.05	.03 (.04)
	(1.42)	(-1.33)	(-.66)	

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
[a]Variables were log transformed; higher values represent poorer health.
* $p < .05$, ** $p < .01$, *** $p < .001$.
BMI = Body Mass Index. SCI = Social Competence Interview. SBP = Systolic Blood Pressure.

Table 9. Interaction of Background Life Stress, Diastolic Blood Pressure Recovery, and Group on Health Outcomes.

Predictor variable	Model 1: Perceived General Health [a]	Model 2: Perceived Mental Health [a]	Model 3: Somatic Symptoms	Model 4: Functional Disability
Step 1: Control variables				
Age	.08	-.01	.09	.10
	(1.39)	(-.09)	(1.73)	(1.84)
Sex	-.23***	-.23***	-.24***	-.19***
	(-4.47)	(-4.39)	(-4.68)	(-3.85)
BMI	.10	.05	.09	.13*
	(1.88)	(.93)	(1.62)	(2.35)
Step 2: Predictor variables				
Group	.24***	.09	.22***	.24***
	(4.49)	(1.64)	(4.22)	(4.63)
Background life stress	.17**	.26***	.23***	.18***
	(3.28)	(5.01)	(4.49)	(3.52)
Post-SCI DBP Recovery	.02	.002	.05	.02
	(.41)	(-.03)	(1.09)	(.35)
Step 3: Primary Interactions				
Background life stress X	.07	-.01	.04	.05
Reactivity	(1.29)	(-.11)	(.73)	(1.06)
Step 4: Secondary Interactions				
Background life stress X	-.05	-.03	.05	.10
Group	(-.61)	(-.36)	(.65)	(1.22)
Group X Recovery	.09	-.09	.03	.10
	(1.15)	(-1.05)	(.41)	(1.32)
Step 5: Three-Way Interaction				
Background life stress X	-.05	-.003	-.03	.08
Reactivity X Group	(-.69)	(-.04)	(-.41)	(1.11)

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
[a]Variables were log transformed; higher values represent poorer health.
* $p < .05$, ** $p < .01$, *** $p < .001$.
BMI = Body Mass Index. SCI = Social Competence Interview. DBP = Diastolic Blood Pressure.

Relation of Background Life Stress and Health Outcomes

A series of hierarchical multiple regression analyses were conducted to test the hypothesis that greater background life stress would be associated with poorer health outcomes, particularly for those with a history of childhood FAP (see Table 10). Controlling for age, sex, and BMI, greater background life stress was associated with poorer perceived physical health ($\beta = 0.17$, $p = .001$), poorer perceived mental health ($\beta = 0.27$, $p < .001$), greater somatic symptoms ($\beta = 0.21$, $p < .001$), and higher levels of functional disability ($\beta = 0.18$, $p = .001$). Those with a history of childhood FAP had significantly poorer general and mental health, greater somatic symptoms, and greater functional disability than healthy controls. There were no significant interactions of background life stress and group on health outcomes.

Table 10. Interaction of Background Life Stress and Group on Health Outcomes.

Predictor variable	Model 1: Perceived General Health [a]	Model 2: Perceived Mental Health [a]	Model 3: Somatic Symptoms	Model 4: Functional Disability
Step 1: Control variables				
Age	.06	-.01	.07	.09
	(1.21)	(-.13)	(1.28)	(1.61)
Sex	-.23***	-.23***	-.23***	-.19***
	(-4.84)	(-4.53)	(-4.45)	(-3.81)
BMI	.13*	.04	.09	.14*
	(2.44)	(.80)	(1.63)	(2.58)
Step 2: Predictor variables				
Group	.23***	.09	.20***	.25***
	(4.47)	(1.80)	(3.96)	(4.84)
Background life stress	.17**	.27***	.21***	.18**
	(3.46)	(5.27)	(4.14)	(3.49)
Step 3: Interactions				
Background life stress X Group	-.04	-.05	.04	.09
	(-.53)	(-.64)	(.54)	(1.07)

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
[a]Variables were log transformed; higher values represent poorer health..
* p < .05, ** p < .01, *** p < .001.
BMI = Body Mass Index.

Relation of Background Life Stress and Cardiovascular Responses

Hierarchical multiple regression analyses controlling for age, sex, and BMI were conducted to examine the relation of background life stress to cardiovascular reactivity and recovery for participants with and without a history of childhood FAP.

Background Life Stress and Baseline Blood Pressure

Background life stress and group were not significant predictors of baseline BP (see Table 11). Interactions between background life stress and group were not significant.

Table 11. Interaction of Background Life Stress and Group on Baseline Blood Pressure.

Predictor variable	Model 1: Baseline SBP	Model 2: Baseline DBP
Step 1: Control variables		
Age	.03	.37***
	(.61)	(6.89)
Sex	.45***	.01
	(9.83)	(.25)
BMI	.29***	-.08
	(6.08)	(-1.51)
Step 2: Predictor variables		
Group	.08	.01
	(1.75)	(.13)
Background life stress	-.03	.01
	(-.67)	(.17)
Step 3: Interactions		
Background life stress X	.02	.14
Group	(.31)	(1.65)

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
* p < .05, ** p < .01, *** p < .001.
SBP = Systolic Blood Pressure. DBP = Systolic Blood Pressure. SCI = Social Competence Interview. SS = Serial Subtraction. BMI = Body Mass Index.

Background Life Stress and Cardiovascular Reactivity

Controlling for age, sex, and BMI, background life stress was not significantly related to SCI or SS reactivity (see Table 12). Groups differed significantly on SCI DBP reactivity ($\beta = -0.14$, $p = .02$), SS SBP reactivity ($\beta = -0.11$, $p < .05$), and SS DBP reactivity ($\beta = -0.14$, $p = .009$). Those with a history of childhood FAP had smaller blood pressure changes than healthy controls. Interactions between background life stress and group were not significant predictors of reactivity.

Table 12. Interaction of Background Life Stress and Group on Cardiovascular Reactivity.

Predictor variable	Model 1: SCI SBP Reactivity	Model 2: SCI DBP Reactivity	Model 3: SS SBP Reactivity	Model 4: SS DBP Reactivity
Step 1: Control variables				
Age	-.02	-.08	.04	-.002
	(-.44)	(-1.50)	(.73)	(-.04)
Sex	-.17**	.06	.29***	.20***
	(-3.18)	(1.13)	(5.62)	(3.92)
BMI	-.21***	-.14	-.12*	-.14*
	(-3.76)	(-2.50)	(-2.27)	(-2.56)
Step 2: Predictor variables				
Group	-.05	-.14*	-.11*	-.14**
	(-.84)	(-2.45)	(-1.98)	(-2.64)
Background life stress	.04	.001	-.07	-.04
	(.73)	(.01)	(-1.42)	(-.69)
Step 3: Interactions				
Background life stress X Group	-.05	-.02	.04	.06
	(-.58)	(-.20)	(.42)	(.69)

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
* p < .05, ** p < .01, *** p < .001.
SCI = Social Competence Interview. SBP = Systolic Blood Pressure. DBP = Systolic Blood Pressure. SS = Serial Subtraction. BMI = Body Mass Index.

Background Life Stress and Cardiovascular Recovery

Controlling for age, sex, and BMI, background life stress was not significantly related to recovery scores (see Table 13). Groups differed significantly on DBP recovery ($\beta = -0.11$, $p < .05$). Those with a history of childhood FAP had slower recovery than healthy controls (i.e., less return to baseline). The interactions between background life stress and group were not significant predictors of recovery.

Table 13. Interaction of Background Life Stress and Group on Cardiovascular Recovery.

Predictor variable	Model 1: SBP Recovery	Model 2: DBP Recovery
Step 1: Control variables		
Age	.07	.12*
	(1.22)	(2.06)
Sex	.14*	-.01
	(2.57)	(-.22)
BMI	.01	-.19**
	(.09)	(-3.39)
Step 2: Predictor variables		
Group	-.05	-.11*
	(-.80)	(-2.01)
Background life stress	.06	.03
	(1.14)	(.54)
Step 3: Interactions		
Background life stress X Group	.05	.07
	(.53)	(.76)

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
* p < .05, ** p < .01, *** p < .001.
SBP = Systolic Blood Pressure. DBP = Systolic Blood Pressure. BMI = Body Mass Index.

Cardiovascular Reactivity and Health Outcomes.

Controlling for age, sex, and BMI, reactivity to the SCI was not significantly related to health outcomes (see Tables 14-17) nor were interactions between SCI reactivity and group significant. Controlling for age, sex, BMI, and group, smaller DBP changes from baseline to the SS task were significantly related to greater functional disability ($\beta = -0.11$, $p < .05$).

Table 14. SCI Systolic Blood Pressure Reactivity by Group on Health Outcomes.

Predictor variable	Model 1: Perceived General Health [a]	Model 2: Perceived Mental Health [a]	Model 3: Somatic Symptoms	Model 4: Functional Disability
Step 1: Control variables				
Age	.09	.01	.11*	.11*
	(1.70)	(.09)	(2.07)	(2.01)
Sex	-.22***	-.23***	-.23***	-.19***
	(-4.28)	(-4.30)	(-4.42)	(-3.71)
BMI	.11*	.05	.09	.13*
	(2.01)	(.86)	(1.65)	(2.39)
Step 2: Predictor variables				
Group	.23***	.10	.22***	.25***
	(4.41)	(1.91)	(4.19)	(4.73)
SCI SBP Reactivity	.00	.07	.002	-.04
	(.07)	(1.22)	(.56)	(-.74)
Step 3: Interactions				
Reactivity X Group	.03	.09	.01	.04
	(.38)	(1.05)	(.16)	(.48)

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
[a]Variables were log transformed; higher values represent poorer health.
* p < .05, ** p < .01, *** p < .001.
BMI = Body Mass Index. SCI = Social Competence Interview. SBP = Systolic Blood Pressure.

Table 15. SCI Diastolic Blood Pressure Reactivity by Group on Health Outcomes.

Predictor variable	Model 1: Perceived General Health [a]	Model 2: Perceived Mental Health [a]	Model 3: Somatic Symptoms	Model 4: Functional Disability
Step 1: Control variables				
Age	.09	.01	.11*	.11*
	(1.70)	(.09)	(2.10)	(2.01)
Sex	-.22***	-.23***	-.23***	-.19***
	(-4.28)	(-4.30)	(-4.42)	(-3.71)
BMI	.11*	.05	.09	.13*
	(2.01)	(.86)	(1.65)	(2.39)
Step 2: Predictor variables				
Group	.24***	.11*	.22***	.25***
	(4.50)	(2.07)	(4.09)	(4.65)
SCI DBP Reactivity	.05	.10	-.02	-.02
	(.88)	(1.76)	(-.47)	(-.40)
Step 3: Interactions				
Reactivity X Group	-.08	.08	.05	.11
	(-1.01)	(.96)	(.65)	(1.32)

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
[a]Variables were log transformed; higher values represent poorer health.
* p < .05, ** p < .01, *** p < .001.
BMI = Body Mass Index. SCI = Social Competence Interview. DBP = Diastolic Blood Pressure.

Table 16. SS Systolic Blood Pressure Reactivity by Group on Health Outcomes.

Predictor variable	Model 1: Perceived General Health [a]	Model 2: Perceived Mental Health [a]	Model 3: Somatic Symptoms	Model 4: Functional Disability
Step 1: Control variables				
Age	.08	.003	.11	.11*
	(1.44)	(.05)	(1.93)	(1.99)
Sex	-.23***	-.22***	-.23***	-.19***
	(-4.38)	(-4.28)	(-4.43)	(-3.63)
BMI	.10	.05	.09	.13*
	(1.88)	(.86)	(1.56)	(2.34)
Step 2: Predictor variables				
Group	.24***	.11	.22***	.24***
	(4.58)	(1.95)	(4.07)	(4.54)
SS SBP Reactivity	.00	.06	-.09	-.10
	(-.003)	(1.07)	(-1.69)	(-1.86)
Step 3: Interactions				
Reactivity X Group	.12	-.04	.12	.10
	(1.43)	(-.43)	(1.39)	(1.17)

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
[a]Variables were log transformed; higher values represent poorer health.
* $p < .05$, ** $p < .01$, *** $p < .001$.
BMI = Body Mass Index. SS = Serial Subtraction. SBP = Systolic Blood Pressure.

Table 17. SS Diastolic Blood Pressure Reactivity by Group on Health Outcomes.

Predictor variable	Model 1: Perceived General Health [a]	Model 2: Perceived Mental Health [a]	Model 3: Somatic Symptoms	Model 4: Functional Disability
Step 1: Control variables				
Age	.08	.003	.11	.11*
	(1.44)	(.05)	(1.93)	(1.99)
Sex	-.23***	-.22***	-.23***	-.19***
	(-4.38)	(-4.28)	(-4.43)	(-3.63)
BMI	.10	.05	.09	.13*
	(1.88)	(.86)	(1.56)	(2.34)
Step 2: Predictor variables				
Group	.25***	.10	.22***	.23***
	(4.63)	(1.80)	(4.07)	(4.42)
SS DBP Reactivity	.03	-.01	-.06	-.11*
	(.54)	(-.19)	(-1.17)	(-2.19)
Step 3: Interactions				
Reactivity X Group	.01	-.12	.04	.12
	(.12)	(-1.32)	(.45)	(1.42)

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
[a]Variables were log transformed; higher values represent poorer health.
* p < .05, ** p < .01, *** p < .001.
BMI = Body Mass Index. SS = Serial Subtraction. DBP = Diastolic Blood Pressure.

Cardiovascular Recovery and Health Outcomes

Controlling for age, sex, and BMI, post-SCI BP recovery was not significantly related to health outcomes (see Tables 18-19). Interactions between recovery and group were not significant.

Table 18. Systolic Blood Pressure Recovery by Group on Health Outcomes.

Predictor variable	Model 1: Perceived General Health [a]	Model 2: Perceived Mental Health [a]	Model 3: Somatic Symptoms	Model 4: Functional Disability
Step 1: Control variables				
Age	.08	-.01	.09	.10
	(1.39)	(-.09)	(1.73)	(1.84)
Sex	-.23***	-.23***	-.24***	-.20***
	(-4.47)	(-4.39)	(-4.68)	(-3.85)
BMI	.10	.05	.09	.13*
	(1.88)	(.93)	(1.62)	(2.35)
Step 2: Predictor variables				
Group	.24***	.11	.23***	.25***
	(4.60)	(1.95)	(4.40)	(4.82)
Post-SCI SBP	-.06	.03	.09	.03
Recovery	(-1.25)	(.50)	(1.69)	(.59)
Step 3: Interactions				
Recovery X Group	.11	-.02	.10	.10
	(1.37)	(-.21)	(1.22)	(1.24)

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
[a]Variables were log transformed; higher values represent poorer health.
* p < .05, ** p < .01, *** p < .001.
BMI = Body Mass Index. SCI = Social Competence Interview. SBP = Systolic Blood Pressure.

Table 19. Diastolic Blood Pressure Recovery by Group on Health Outcomes.

Predictor variable	Model 1: Perceived General Health [a]	Model 2: Perceived Mental Health [a]	Model 3: Somatic Symptoms	Model 4: Functional Disability
Step 1: Control variables				
Age	.08	-.01	.09	.10
	(1.39)	(-.09)	(1.73)	(1.84)
Sex	-.23***	-.23***	-.24***	-.20***
	(-4.47)	(-4.39)	(-4.68)	(-3.85)
BMI	.10	.05	.09	.13*
	(1.88)	(.93)	(1.62)	(2.35)
Step 2: Predictor variables				
Group	.25***	.11	.23***	.26***
	(4.67)	(1.94)	(4.43)	(4.82)
Post-SCI DBP	.03	.01	.06	-.08
Recovery	(.49)	(.11)	(1.19)	(-.97)
Step 3: Interactions				
Recovery X Group	.12	-.07	.06	.13
	(1.49)	(-.85)	(.72)	(1.67)

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
[a]Variables were log transformed; higher values represent poorer health.
* p < .05, ** p < .01, *** p < .001.
BMI = Body Mass Index. SCI = Social Competence Interview. DBP = Diastolic Blood Pressure.

Childhood Family Stress

Childhood family stress was not a significant predictor of health status in adolescence and adulthood (see Table 20). Two-way interactions between childhood life stress and background life stress were not significant predictors of health status.

Table 20. Interaction of Background Life Stress and Childhood Family Stress on Health Outcomes.

Predictor variable	Model 1: Perceived General Health [a]	Model 2: Perceived Mental Health [a]	Model 3: Somatic Symptoms	Model 4: Functional Disability
Step 1: Control variables				
Age	.03	-.04	-.02	.04
	(.45)	(-.49)	(-.29)	(.51)
Sex	-.15*	-.15*	-.21**	-.16*
	(-2.01)	(-2.02)	(-2.93)	(-2.13)
BMI	.14	.06	.12	.17*
	(1.84)	(.78)	(1.59)	(2.32)
Step 2: Predictor variables				
Background life stress	.20**	.25**	.26***	.18*
	(2.64)	(3.25)	(3.56)	(2.42)
Childhood family stress	-.04	-.03	.08	.10
	(-.54)	(-.40)	(1.04)	(1.41)
Step 3: Two-Way Interaction				
Background life stress X	-.01	.01	.01	.11
Childhood family stress	(-.14)	(.13)	(.13)	(1.52)

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
[a]Variables were log transformed; higher values represent poorer health.
* $p < .05$, ** $p < .01$, *** $p < .001$.
BMI = Body Mass Index.

Childhood life stress was not a significant predictor of cardiovascular reactivity (see Table 21). Two-way interactions between childhood life stress and background life stress were not significant predictors of cardiovascular reactivity.

Table 21. Interaction of Background Life Stress and Childhood Family Stress on Cardiovascular Reactivity.

Predictor variable	Model 1: SCI SBP Reactivity	Model 2: SCI DBP Reactivity	Model 3: SS SBP Reactivity	Model 4: SS DBP Reactivity
Step 1: Control variables				
Age	.02	.01	.04	-.02
	(.28)	(.16)	(.47)	(-.20)
Sex	.22**	.04	.29***	.15
	(2.99)	(.49)	(3.97)	(1.94)
BMI	-.11	-.002	-.08	-.10
	(-1.39)	(-.03)	(-1.03)	(-1.31)
Step 2: Predictor variables				
Background life stress	.06	.03	-.01	.02
	(.82)	(.37)	(-.13)	(.22)
Childhood family stress	-.15	-.15	-.11	.08
	(-1.88)	(-1.83)	(-1.46)	(.99)
Step 3: Interactions				
Background life stress X Childhood family stress	-.04	-.03	.09	.02
	(-.57)	(-.33)	(1.21)	(.23)

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
* $p < .05$, ** $p < .01$, *** $p < .001$.
BMI = Body Mass Index. SCI = Social Competence Interview. SBP = Blood Pressure. DBP = Diastolic Blood Pressure. SS = Serial Subtraction.

Childhood family stress was not a significant predictor of post-SCI cardiovascular recovery (see Table 22). Two-way interactions between childhood life stress and background life stress were not significant predictors of cardiovascular recovery.

Table 22. Interaction of Background Life Stress and Childhood Family Stress on Cardiovascular Recovery.

Predictor variable	Model 1: Post-SCI SBP Recovery	Model 2: Post-SCI DBP Recovery
Step 1: Control variables		
Age	.04	.12
	(.44)	(1.57)
Sex	.12	-.01
	(1.61)	(-.09)
BMI	.10	-.17*
	(1.21)	(-2.14)
Step 2: Predictor variables		
Background life stress	.13	.13
	(1.58)	(1.60)
Childhood family stress	-.03	-.03
	(-.36)	(-.36)
Step 3: Interactions		
Background life stress X Childhood family stress	.11	.07
	(1.42)	(.86)

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
* p < .05, ** p < .01, *** p < .001.
SCI = Social Competence Interview. BMI = Body Mass Index. SBP = Blood Pressure. DBP = Diastolic Blood Pressure.

There was a significant three-way interaction among background life stress, childhood family stress, and SBP reactivity to the SCI task on somatic symptoms ($\beta = -0.23$, $p < .01$) among those with a history of childhood FAP (see Table 23). Among those with high childhood family stress, increased background life stress was not associated with somatic symptoms at low or high levels of SBP reactivity to the SCI. Among those with low childhood family stress, increased background life stress was associated with increased somatic symptoms, particularly among those with high SBP reactivity to the SCI.

Table 23. Interaction of Background Life Stress, Childhood Family Stress, and SCI Systolic Blood Pressure Reactivity on Health Outcomes.

Predictor variable	Model 1: Perceived General Health [a]	Model 2: Perceived Mental Health [a]	Model 3: Somatic Symptoms	Model 4: Functional Disability
Step 1: Control variables				
Age	.05	-.01	.02	.07
	(.57)	(-.08)	(.25)	(.86)
Sex	-.15*	-.13	-.20**	-.16*
	(-1.99)	(-1.76)	(-2.69)	(-2.12)
BMI	.11	.05	.15	.17*
	(1.38)	(.61)	(1.92)	(2.17)
Step 2: Predictor variables				
Background life stress	.19*	.24**	.30***	.21**
	(2.49)	(3.05)	(4.12)	(2.73)
Childhood Family	-.03	-.04	.06	.10
Stress	(-.39)	(-.45)	(.78)	(1.38)
SCI SBP reactivity	.03	.06	.01	-.02
	(.41)	(.80)	(.08)	(-.28)
Step 3: Two-Way Interactions				
Background life stress X	.001	.04	.02	.13
Childhood family stress	(.02)	(.53)	(.21)	(1.66)
Background life stress X	.08	.10	.12	.13
Reactivity	(1.03)	(1.28)	(1.60)	(1.73)
Childhood family stress	-.01	-.004	-.02	-.02
X Reactivity	(-.07)	(-.05)	(-.24)	(-.32)
Step 5: Three-Way Interaction				
Background life stress X	-.05	-.09	-.23**	-.15
Childhood Family Stress	(-.66)	(-1.08)	(-3.04)	(-1.91)
X Reactivity				

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
[a]Variables were log transformed; higher values represent poorer health.
* p < .05, ** p < .01, *** p < .001.
BMI = Body Mass Index. SCI = Social Competence Interview. SBP = Blood Pressure.

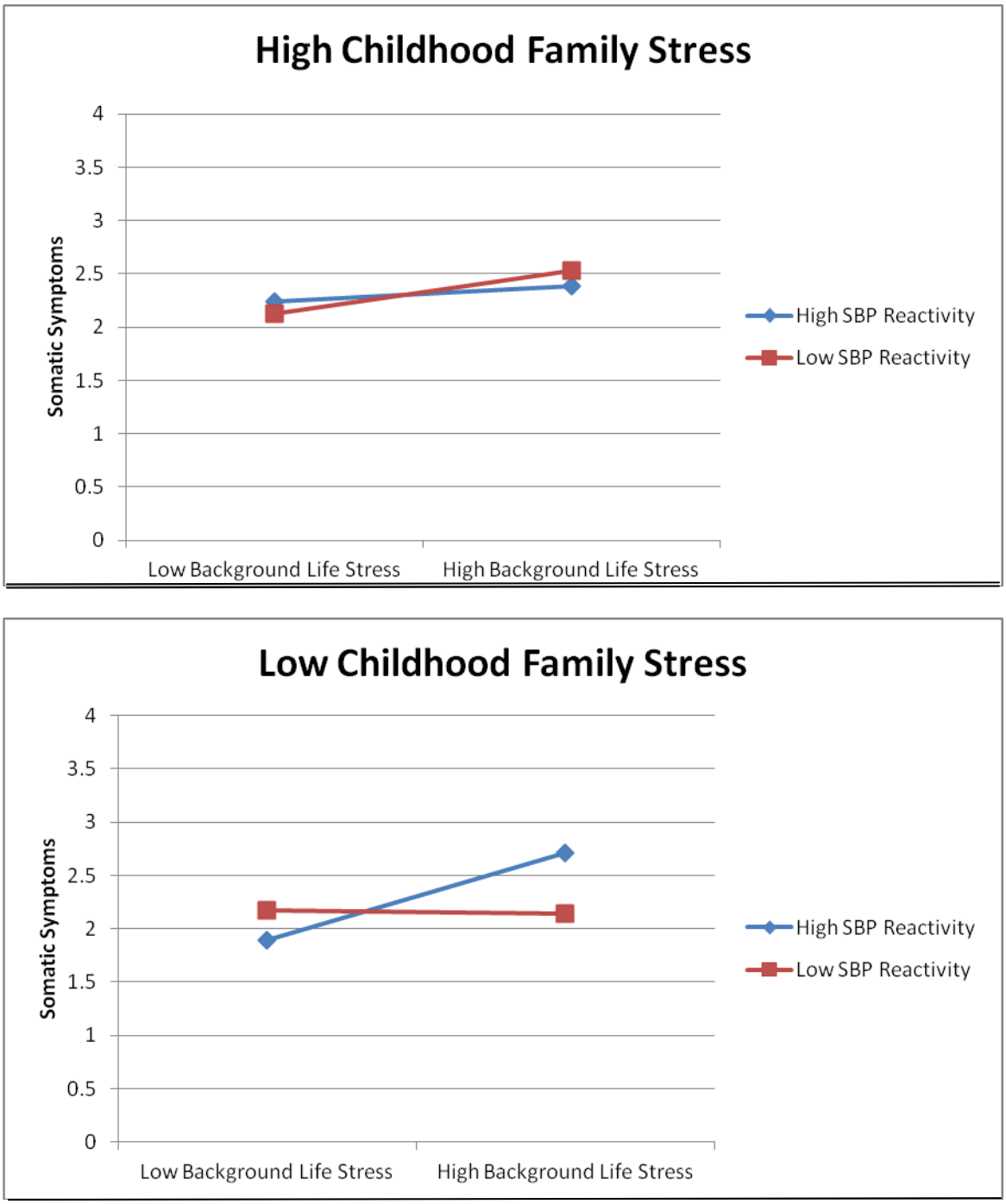


Figure 4. Regression lines showing predicted levels of somatic symptoms for participants with low (-1 SD) and high (+1 SD) childhood family stress with low (-1 SD) and high (+1 SD) SBP reactivity at low (-1 SD) and high (+1 SD) levels of background life stress, controlling for age, sex, and BMI.

There was a significant three-way interaction among background life stress, childhood family stress, and DBP reactivity to the SCI task on somatic symptoms ($\beta = -0.18$, $p < .05$) (see Table 24). The interaction effect was similar to SBP reactivity. Among those with high childhood family stress, increased background life stress was not associated with somatic symptoms at low or high levels of DBP reactivity to the SCI. Among those with low childhood family stress, increased background life stress was associated with increased somatic symptoms, particularly among those with high DBP reactivity to the SCI.

Table 24. Interaction of Background Life Stress, Childhood Family Stress, and SCI Diastolic Blood Pressure Reactivity on Health Outcomes.

Predictor variable	Model 1: Perceived General Health [a]	Model 2: Perceived Mental Health [a]	Model 3: Somatic Symptoms	Model 4: Functional Disability
Step 1: Control variables				
Age	.05	-.01	.02	.07
	(.57)	(-.08)	(.25)	(.86)
Sex	-.15*	-.13	-.20**	-.16*
	(-1.99)	(-1.76)	(-2.69)	(-2.12)
BMI	.11	.05	.15	.17*
	(1.38)	(.61)	(1.92)	(2.17)
Step 2: Predictor variables				
Background life stress	.19*	.24**	.30***	.20**
	(2.51)	(3.09)	(4.13)	(2.71)
Childhood Family	-.03	-.03	.06	.11
Stress	(-.44)	(-.37)	(.76)	(1.47)
SCI DBP reactivity	.004	.11	-.004	.03
	(.06)	(1.49)	(-.05)	(.37)
Step 3: Two-Way Interactions				
Background life stress X	-.01	.03	-.01	.11
Childhood family stress	(-.18)	(.34)	(-.13)	(1.45)
Background life stress X	.03	.08	.04	.10
Reactivity	(.34)	(.93)	(.50)	(1.25)
Childhood family stress	-.03	-.12	-.09	-.12
X Reactivity	(-.37)	(-1.53)	(-1.16)	(-1.60)
Step 5: Three-Way Interaction				
Background life stress X	-.10	-.10	-.18*	-.11
Childhood Family Stress	(-1.25)	(-1.21)	(-2.40)	(-1.40)
X Reactivity				

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
[a]Variables were log transformed; higher values represent poorer health.
* p < .05, ** p < .01, *** p < .001.
BMI = Body Mass Index. SCI = Social Competence Interview. DBP = Diastolic Blood Pressure. SS = Serial Subtraction.

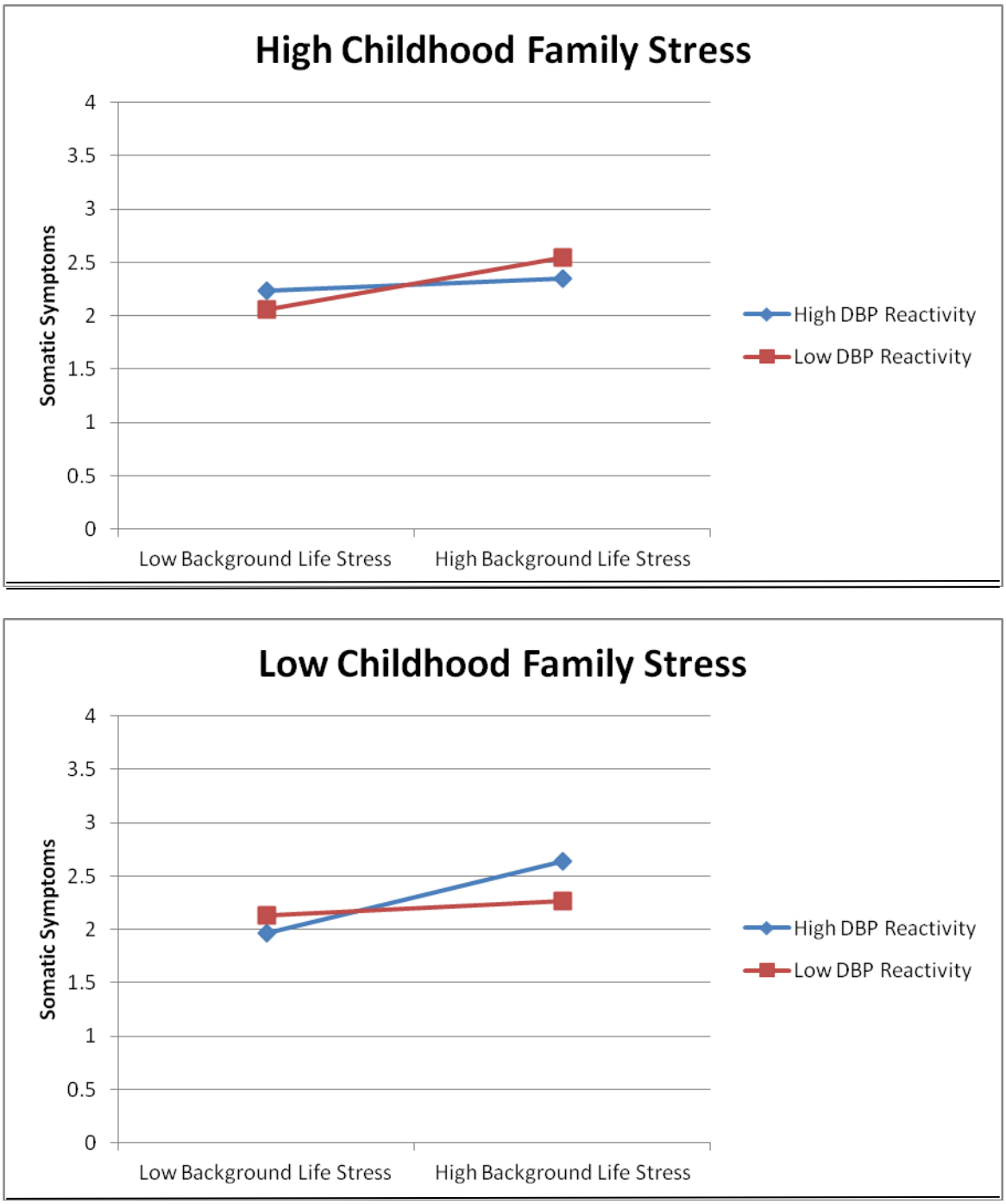


Figure 4. Interaction of background life stress, childhood family stress, and SCI diastolic reactivity on somatic symptoms.

Interactions of childhood life stress, background life stress, and SS BP reactivity were not significant predictors of symptoms (Tables 25-26).

Table 25. Interaction of Background Life Stress, Childhood Family Stress, and SS Systolic Blood Pressure Reactivity on Health Outcomes.

Predictor variable	Model 1: Perceived General Health [a]	Model 2: Perceived Mental Health [a]	Model 3: Somatic Symptoms	Model 4: Functional Disability
Step 1: Control variables				
Age	.05	-.10	.02	.07
	(.57)	(-.08)	(.25)	(.87)
Sex	-.15*	-.13	-.20**	-.15*
	(-1.97)	(-1.74)	(-.264)	(-2.06)
BMI	.10	.05	.13	.15
	(1.30)	(.57)	(1.72)	(1.93)
Step 2: Predictor variables				
Background life stress	.19*	.24**	.30***	.20**
	(2.51)	(3.08)	(4.09)	(2.67)
Childhood Family	-.03	-.04	.06	.11
Stress	(-.33)	(-.55)	(.82)	(1.46)
SS SBP reactivity	.08	.01	.02	.001
	(1.01)	(.12)	(.31)	(.01)
Step 3: Two-Way Interactions				
Background life stress X	-.03	.02	-.02	.10
Childhood family stress	(-.33)	(.22)	(-.24)	(1.31)
Background life stress X	-.06	-.04	-.04	.002
SS systolic reactivity	(-.71)	(-.50)	(-.45)	(.02)
Childhood family stress	-.09	-.07	-.02	-.01
X SS systolic reactivity	(-.99)	(-.84)	(-.22)	(-.16)
Step 5: Three-Way Interaction				
Background life stress X	.08	-.06	-.04	-.12
Childhood Family Stress	(.77)	(-.57)	(-.44)	(-1.26)
X SS systolic reactivity				

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
[a]Variables were log transformed; higher values represent poorer health.
* $p < .05$, ** $p < .01$, *** $p < .001$.
BMI = Body Mass Index. SS = Serial Subtraction. SBP = Blood Pressure.

Table 26. Interaction of Background Life Stress, Childhood Family Stress, and SS Diastolic Reactivity on Health Outcomes.

Predictor variable	Model 1: Perceived General Health [a]	Model 2: Perceived Mental Health [a]	Model 3: Somatic Symptoms	Model 4: Functional Disability
Step 1: Control variables				
Age	.05	-.01	.02	.07
	(.57)	(-.08)	(.25)	(.87)
Sex	-.15*	-.13	-.20**	-.15*
	(-1.97)	(-1.74)	(-2.64)	(-2.06)
BMI	.10	.05	.13	.15
	(1.30)	(.57)	(1.72)	(1.93)
Step 2: Predictor variables				
Background life stress	.19*	.24**	.30***	.20**
	(2.50)	(3.12)	(4.10)	(2.67)
Childhood Family Stress	-.03	-.04	.06	.11
	(-.42)	(-.46)	(.82)	(1.48)
SS DBP reactivity	-.02	-.11	-.03	-.02
	(-.31)	(-1.40)	(-.37)	(-.24)
Step 3: Two-Way Interactions				
Background life stress X Childhood family stress	-.001	.05	-.003	.12
	(-.01)	(.58)	(-.04)	(1.58)
Background life stress X Reactivity	.08	.06	-.01	.15
	(1.01)	(.79)	(-.18)	(1.93)
Childhood family stress X Reactivity	-.12	-.19*	-.06	-.13
	(-1.53)	(-2.49)	(-.85)	(-1.74)
Step 5: Three-Way Interaction				
Background life stress X Childhood Family Stress X Reactivity	-.01	-.07	-.03	.003
	(-.14)	(-.80)	(-.32)	(.04)

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
[a]Variables were log transformed; higher values represent poorer health.
* $p < .05$, ** $p < .01$, *** $p < .001$.
BMI = Body Mass Index. SS = Serial Subtraction. DBP = Diastolic Blood Pressure.

Interactions of childhood life stress, background life stress, and post-SCI BP recovery were not significant predictors of symptoms (Tables 27-28).

Table 27. Interaction of Background Life Stress, Childhood Family Stress, and Systolic Recovery on Health Outcomes.

Predictor variable	Model 1: Perceived General Health [a]	Model 2: Perceived Mental Health [a]	Model 3: Somatic Symptoms	Model 4: Functional Disability
Step 1: Control variables				
Age	.05	-.01	.02	.07
	(.57)	(-.08)	(.25)	(.86)
Sex	-.15*	-.13	-.20**	-.16*
	(1.99)	(-1.76)	(-2.69)	(-2.12)
BMI	.11	.05	.15	.17*
	(1.38)	(.61)	(1.92)	(2.17)
Step 2: Predictor variables				
Background life stress	.20*	.25**	.29***	.21**
	(2.56)	(3.15)	(3.98)	(2.72)
Childhood Family	-.04	-.05	.06	.11
Stress	(-.47)	(-.58)	(.81)	(1.43)
Post-SCI SBP recovery	-.04	-.05	.08	-.01
	(-.50)	(-.59)	(1.17)	(-.18)
Step 3: Two-Way Interactions				
Background life stress X	.12	.09	.06	.02
Childhood family stress	(1.49)	(1.14)	(.75)	(.27)
Background life stress X	.03	.05	-.03	.06
SBP recovery	(.36)	(.59)	(-.35)	(.72)
Childhood family stress	-.16	-.10	.01	.14
X SBP recovery	(-1.86)	(-1.15)	(.13)	(1.68)
Step 5: Three-Way Interaction				
Background life stress X	-.02	-.02	-.07	.02
Childhood Family Stress	(-.24)	(-.20)	(-.90)	(.19)
X SBP recovery				

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
[a]Variables were log transformed; higher values represent poorer health.
* p < .05, ** p < .01, *** p < .001.
BMI = Body Mass Index. SCI = Social Competence Interview. SBP = Systolic Blood Pressure.

Table 28. Interaction of Background Life Stress, Childhood Family Stress, and Diastolic Recovery on Health Outcomes.

Predictor variable	Model 1: Perceived General Health [a]	Model 2: Perceived Mental Health [a]	Model 3: Somatic Symptoms	Model 4: Functional Disability
Step 1: Control variables				
Age	.05	-.01	.02	.07
	(.57)	(-.08)	(.25)	(.86)
Sex	-.15*	-.13	-.20**	-.16*
	(-1.99)	(-1.76)	(-2.69)	(-2.12)
BMI	.11	.05	.15	.17*
	(1.38)	(.61)	(1.92)	(2.17)
Step 2: Predictor variables				
Background life stress	.19*	.25**	.29***	.20*
	(-.44)	(3.17)	(3.98)	(2.62)
Childhood Family	-.03	-.05	.06	.11
Stress	(-.44)	(-.59)	(.81)	(1.46)
Post-SCI DBP recovery	.04	-.06	.08	.05
	(.52)	(-.75)	(1.11)	(.69)
Step 3: Two-Way Interactions				
Background life stress X	.05	.06	.04	.15*
Childhood family stress	(.64)	(.77)	(.58)	(2.02)
Background life stress X	-.01	.04	.01	.10
DBP recovery	(-.16)	(.50)	(.10)	(1.26)
Childhood family stress	-.04	-.08	-.10	-.04
X DBP recovery	(-.49)	(-1.05)	(-1.33)	(-.56)
Step 5: Three-Way Interaction				
Background life stress X	.01	-.04	.12	.04
Childhood Family Stress	(.14)	(-.49)	(1.56)	(.59)
X DBP recovery				

Notes: The values shown are standardized beta coefficients. *t* statistics in parentheses.
[a]Variables were log transformed; higher values represent poorer health.
* p < .05, ** p < .01, *** p < .001.
BMI = Body Mass Index. SCI = Social Competence Interview. DBP = Diastolic Blood Pressure.

CHAPTER V

DISCUSSION

This study explored relations among background life stress, cardiovascular responses to laboratory stressors, and health outcomes in adolescence and young adulthood among individuals with and without a history of childhood FAP. Previous research has demonstrated a relation between daily stressors and somatic symptoms in FAP (Walker, et al., 2001). However, moderating or contributing factors in the association between background life stress and indices of health have not been adequately examined in previous research. In this study, physiologic responses to acute stress, operationalized as cardiovascular reactivity to and recovery from laboratory stress tasks, were examined as potential moderators of the relation between background life stress and the health outcomes. In addition, pathways linking background life stress, cardiovascular responses to laboratory stress, and symptoms cross-sectionally were evaluated for evidence of cardiovascular responses to laboratory stress as a potential indirect path between background life stress and health outcomes.

Prior to discussing findings related to the primary study hypotheses, several core findings of the current study are of interest as they extend the literature on differences between FAP and healthy controls (Campo, et al., 2001; McGrath, et al., 1983; Walker, et al., 1995). Prior research has demonstrated that youth with FAP report higher levels of background life stress than healthy controls. This study showed that individuals with a history of childhood FAP continued to report higher levels of life stress than controls when they reached young adulthood. Similarly, this study found that poor health, as indicated by greater functional disability, a higher level of

somatic symptoms, poorer perceived mental health, and poorer perceived overall general health, continued to characterize those with a history of FAP compared to controls years after their initial evaluation in childhood. These findings are consistent with those of several other studies reporting poor long-term health outcomes for individuals with a history of FAP (Campo, et al., 2001; Hotopf & Carr, 1998; Mulvaney, et al., 2006; Walker, et al., 1995), but have the added strength of a prospective investigation with a healthy comparison group, standardized measures of health outcomes, and evaluation of multiple components of health. Thus, the study provides the strongest evidence to date linking pediatric FAP to adverse health outcomes later in life.

Differences between those with and without a history of childhood FAP were generally not found in cardiovascular responses to laboratory stress when evaluated in adolescence and young adulthood. As measured by blood pressure during a baseline assessment period in the laboratory, basal cardiovascular functioning did not differ between childhood FAP and healthy controls. During two laboratory stress tasks (the Social Competence Interview and the serial subtraction task), both childhood FAP and healthy controls demonstrated the expected increases in blood pressure, and both groups returned to baseline blood pressure levels in the post-stressor recovery period. Investigations of cardiovascular responses to laboratory stress in FAP to date have demonstrated significant differences in heart rate responses to laboratory stressors between children with FAP and healthy controls (Dorn, et al., 2003; Dufton, et al., 2008). However, the present findings suggest that individuals with a history of childhood FAP do not differ from those without a history of childhood FAP in their blood pressure responses to stress when they reach young adulthood. Whether they differed in childhood when they were initially evaluated for FAP is unknown and merits further investigation as studies to date have used small samples and have yielded inconsistent results.

Individuals with a history of FAP tended to demonstrate smaller blood pressure increases during both laboratory stress tasks, whereas healthy controls tended to demonstrate greater blood pressure increases to laboratory stress. The magnitude of the differences in reactivity between groups reached significance for diastolic SCI reactivity and for systolic and diastolic reactivity to serial subtraction, indicating blunted reactivity to laboratory stress by the FAP group in comparison to healthy controls. This finding contrasts with that of one study finding heightened systolic blood pressure reactivity in FAP patients in childhood (Dorn, et al., 2003), but is consistent with that of Jørgensen et al. (1993) who found blunted cardiovascular reactivity to laboratory stress in FAP compared with healthy controls. Blunted reactivity may indicate a diminished ability to handle stress or motivational dysregulation (Carroll, Phillips, & Lovallo, 2012)

Regarding blood pressure recovery following laboratory stress, findings indicated a group difference in diastolic blood pressure recovery following the SCI, with those with a history of childhood FAP exhibiting less recovery (i.e., less return to baseline) than healthy controls. This finding was consistent with expectations and may reflect rumination about the stressful experience or poor parasympathetic nervous system functioning. There was no evidence that the degree of recovery from the first task (the SCI) affected blood pressure responses to the second task (serial subtraction) for either group; a follow-up analysis for serial subtraction controlling for post-SCI recovery blood pressure revealed no group differences in serial subtraction blood pressure, suggesting that differences in recovery from the SCI did not affect blood pressure reactivity to serial subtraction. Recovery from serial subtraction was not measured in the current study.

The main effect of background life stress on health outcomes, controlling for potential confounding variables of age, sex, and BMI, was significant for all outcome measures. Standardized regression coefficients ranged from 0.17 to 0.27. Controlling for potential confounds, these findings approximate the reported range of stress-illness correlations of 0.2 to 0.4 noted by Boyce & Chesterman (1990). Given the cross-sectional nature of the study design, causal inferences cannot be made. Higher background life stress may have contributed to increased symptomatology or, alternatively, it may be that increased symptomatology contributed to increased background life stress, for example if physical or mental health negatively affected relationships or school/work performance.

Contrary to expectations, the correlation of background life stress with health outcomes was similar in those with a history of childhood FAP and healthy controls. This finding is consistent with the notion that background life stress is a "non-specific risk factor" that is not exclusive to FAP (Hymowitz, 2011). It may also be that background life stress has a greater influence on symptoms in childhood. Although those with a history of childhood FAP reported higher levels of background life stress and poorer health outcomes, it is important to note that both background life stress and health may be influenced by self-report biases as all outcomes were subjective reports.

One of the most interesting findings of the present study arose from the hypothesis that individual differences in cardiovascular reactivity and recovery following laboratory stress tasks would moderate the associations between background life stress and symptom outcomes. A significant three-way interaction of systolic blood pressure reactivity to the SCI, group, and background life stress was found for perceived general health. Among those with a history of childhood FAP, higher levels of background life stress were associated with poorer perceived

general health, but only for those with high reactivity to the SCI (i.e., greater increases from baseline to the SCI). In contrast, among those with a history of childhood FAP and low reactivity to laboratory stress (i.e., smaller increases or decreasing blood pressure from baseline), background life stress had little relation to perceived general health. Healthy controls had greater perceived general health with the exception of those with low reactivity in the context of high background life stress having poorer perceived general health. These findings for FAP are generally in line with those of prior research indicating that individuals who are "high reactors" under high-stress conditions tend to have greater illness and psychological symptoms (Boyce, et al., 1995; Clements & Turpin, 2000; Cohen, et al., 2002).

To the extent that cardiovascular reactivity to laboratory stress represents an individual's typical, trait-like style of responding to acute stress, these findings are consistent with the diathesis-stress model. In individuals with a history of FAP, cardiovascular reactivity to acute stress may represent an added vulnerability factor that further increases adverse health outcomes in the context of high background life stress. Less reactivity in the face of acute stress may be protective and buffer against the adverse effect of background life stress on health. For individuals with a history of FAP, greater background life stress may tax an individual's coping resources particularly in those with greater reactivity. Therefore, higher reactivity to laboratory stress and greater background life stress may interact to exacerbate adverse health effects associated with either risk factor alone. If these findings can be replicated in other samples, it would be important to examine coping, temperament, negative affect, and social support as additional contributing or moderating factors in the relation between background life stress and health.

Data on childhood family stress as reported by parents at the time of baseline study enrollment were available for participants with a history of childhood FAP. Background life stress was positively and significantly correlated with childhood family stress, although the magnitude of the correlation was only r = 0.28. Childhood family stress did not significantly predict health outcomes either directly or in interaction with background life stress at follow-up. However, there were significant three-way interactions of childhood family stress, background life stress, and both systolic and diastolic blood pressure reactivity to the SCI on level of somatic symptoms at follow-up. The interaction effect suggests that for those with high childhood family stress, there was a smaller relation between background life stress and somatic symptoms without much difference depending on blood pressure reactivity to laboratory stress. When those with low childhood family stress get older and have high reactivity, high background life stress was associated with greater somatic symptoms. These findings ran counter to what was expected and may be an unreliable finding. Should these findings be replicated, it may be that high childhood family stress has an inoculation effect such that higher background life stress later in life does not increase symptoms regardless of the individual's level of reactivity to acute stress (Musante, et al., 2000). Individuals exposed to more stressors for a longer period may have developed coping strategies over time that protect against adverse outcomes, even when psychosocial stress and reactivity are high. Conversely, those with low childhood stress and generally high reactivity may have greater adverse outcomes as a result of poorly developed coping with high levels of more recent background life stress or with the onset of greater stress later in life. These relations warrant further study and replication.

The interaction of group and background life stress was hypothesized to predict cardiovascular reactivity to and recovery from laboratory stressors given that background life

stress load theoretically may play a role in the way individuals with FAP respond to acute stress experiences. Previous research suggests that cumulative exposure to naturally occurring stressors can alter cardiovascular response to both laboratory and environmental challenges (Chida & Hamer, 2008). However, studies to date investigating the effects of background life stress on reactivity have produced mixed results. The present study found no significant main effects for background life stress on cardiovascular reactivity to or recovery from laboratory stress and no group by background life stress interactions. Other studies have also failed to support a direct independent effect of life events on cardiovascular reactivity to laboratory stress (Boyce & Chesterman, 1990; Roy, et al., 1998). It is possible that effects may hold only for more chronic, ongoing, unresolved, and important stressors as found by Matthews and colleagues (1997). The measure of background life stress used in this study did not assess duration of stressor exposure, perceived importance of stressors or whether stressors were ongoing or resolved. While Matthews et al. (1997) purported to measure duration and importance of stressors, they used the SCI which is designed to assess only a single stressor domain in order to elicit cardiovascular responses. Future studies should examine the extent to which other aspects of background life stressors, such as chronicity and valence, are associated with cardiovascular responses. Importantly, this study examined background life stress as a count of stressors, and appraisal of both background life stressors and laboratory stressors is a critical factor that should be examined in future studies.

In this sample, contrary to expectations, cardiovascular reactivity to laboratory stressors was not significantly associated with health outcomes, with the exception that diastolic blood pressure reactivity to serial subtraction was inversely related to functional disability. There were no group by reactivity or recovery interactions, revealing that both groups similarly had no direct

effects of reactivity and recovery on health outcomes. The finding that cardiovascular recovery was not associated with health outcomes also was unexpected, given that failure to adapt rapidly has been suggested to be potentially more important than the initial response (Chida & Hamer, 2008). It is important to note, however, that this study was conducted in a sample of young adults with a history of childhood FAP. Results might differ for children with FAP assessed at the time of their pediatric medical evaluation. It also may be that the relation between cardiovascular responses to acute stress (such as that assessed in the laboratory) and changes in health status develop over a longer period of time.

The results of analyses examining the pathways among background life stress, cardiovascular response, and health outcomes did not yield evidence that cardiovascular response to laboratory stress constituted a significant indirect path between background life stress and health outcomes. While background life stress was associated with health outcomes, background life stress was not associated with cardiovascular response nor was cardiovascular response to stress significantly related to health outcomes. Furthermore, contrary to expectations, relations among these variables did not differ for those with and without a history of childhood FAP. The findings are consistent with reviews that have found fewer positive associations between background life stress and reactivity or recovery when using measures of life events to operationalize background life stress, as opposed to measures that take into account whether stressors have resolved (Gump & Matthews, 1999). Future research should use other methods to assess background life stress, such as semi-structured interviews or measures of daily hassles. In addition, Gump and Matthews (1999) note that the choice of laboratory stressors is important as those of very short duration (such as the 2-minute serial subtraction task in this study) may not allow enough time for the effect of background life stress on magnitude of initial response or

habituation to stress exposure to be revealed. Finally, reactivity to laboratory stress may be tempered by unassessed factors such as hardiness, social support, and coping.

In addition to limitations already noted, the nature of the sample limits the generalizabilty of the present study. Individuals with a history of childhood FAP were recruited from a tertiary care setting, and results may not generalize to FAP recruited in other settings (e.g., community or primary care). This study examined health outcomes in adolescents and young adults with a history of childhood FAP, and findings may differ when FAP is initially evaluated in childhood. The specificity of findings for FAP could be assessed in future studies with the inclusion of a pain control group. It is also of note that this study, like many (Chida & Hamer, 2008), examined only one measure of physiological response to laboratory stress. Neuroendocrine hormonal responses, immune responses, and other cardiovascular indicators aside from blood pressure would be important to assess in future research. Further, the interaction among various physiological systems is an area of need in future research. Attention to the laboratory stressor used and what responses they elicit will be important considerations for such studies. Assessment of health outcomes not solely relying on participant self-report of their symptoms and disability would also add to the literature and empirical evidence of effects of stress and associated physiological responding on health and illness. Consistent with the majority of studies in the literature, the current study did not examine positive outcomes which may be important. Protective and resilience factors therefore can also be examined in future research.

These limitations notwithstanding, the current study provided important findings of differences between those with a history of childhood FAP and healthy controls. Findings demonstrated that individuals with a history of childhood FAP had significantly higher levels of background life stress levels and significantly poorer health outcomes in adolescence and

adulthood as compared to those without a history of childhood FAP. The relations among background life stress, cardiovascular responses to laboratory stress, and health outcomes, however, did not differ between those with and without a history of childhood FAP. Those with a history of childhood FAP and high cardiovascular reactivity to laboratory stress displayed a stronger relation between background life stress and perceived general health as compared to those with childhood FAP and low cardiovascular reactivity to laboratory stress or healthy controls with high cardiovascular reactivity to laboratory stress. Further research examining acute stress reactivity and recovery with assessment of additional physiological systems will further elucidate the role of stress in illness in general, and prospective studies would identify pathways associated with the maintenance of FAP symptoms. Clinically, these results underscore that approaches considering the context of stress and enhancing recovery from stress exposure in FAP are important. A more comprehensive understanding of these associations will strengthen our efforts to effectively prevent and treat functional gastrointestinal disorders.

REFERENCES

Aggarwal, A., Cutts, T., Abell, T., Cardoso, S., Familoni, B., Bremer, J., et al. (1994). Predominant symptoms in irritable bowel syndrome correlate with specific autonomic nervous system abnormalities. *Gastroenterology, 106*(4), 945.

Anda, R., Felitti, V., Bremner, J., Walker, J., Whitfield, C., Perry, B., et al. (2006). The enduring effects of abuse and related adverse experiences in childhood. *European Archives of Psychiatry and Clinical Neuroscience, 256*(3), 174-186.

Bach, D., Erdmann, G., Schmidtmann, M., & Mönnikes, H. (2006). Emotional stress reactivity in irritable bowel syndrome. *European Journal of Gastroenterology and Hepatology, 18*(6), 629-636.

Barr, R., Boyce, W., & Zeltzer, L. (1996). The stress-illness association in children: A perspective from the biobehavioral interface. In R. Haggerty, L. Sherrod, N. Garmezy & M. Rutter (Eds.), *Stress, risk, and resilience in children and adolescents: Processes, mechanisms, and interventions* (pp. 182-224). Cambridge: Cambridge University Press.

Belsky, J., & Pluess, M. (2009). Beyond diathesis stress: Differential susceptibility to environmental influences. *Psychological Bulletin, 135*(6), 885.

Bennett, E., Tennant, C., Piesse, C., Badcock, C., & Kellow, J. (1998). Level of chronic life stress predicts clinical outcome in irritable bowel syndrome. *Gut, 43*(2), 256.

Biggs, A., Aziz, Q., Tomenson, B., & Creed, F. (2003). Do childhood adversity and recent social stress predict health care use in patients presenting with upper abdominal or chest pain? *Psychosomatic Medicine, 65*(6), 1020-1028.

Blanchard, E., Lackner, J., Jaccard, J., Rowell, D., Carosella, A., Powell, C., et al. (2008). The role of stress in symptom exacerbation among IBS patients. *Journal of Psychosomatic Research, 64*(2), 119-128.

Boey, C., & Goh, K. (2001). The significance of life-events as contributing factors in childhood recurrent abdominal pain in an urban community in Malaysia. *Journal of Psychosomatic Research, 51*(4), 559-562.

Boyce, W., Barr, R., & Zeltzer, L. (1992). Temperament and the psychobiology of childhood stress. *Pediatrics, 90*(3), 483-486.

Boyce, W., Chesney, M., Alkon, A., Tschann, J., Adams, S., Chesterman, B., et al. (1995). Psychobiologic reactivity to stress and childhood respiratory illnesses: Results of two prospective studies. *Psychosomatic Medicine, 57*(5), 411-422.

Boyce, W., & Chesterman, E. (1990). Life events, social support, and cardiovascular reactivity in adolescence. *Journal of Developmental & Behavioral Pediatrics, 11*(3), 105-111.

Boyce, W., & Ellis, B. (2005). Biological sensitivity to context: I. An evolutionary–developmental theory of the origins and functions of stress reactivity. *Development and Psychopathology, 17*(02), 271-301.

Boyce, W., & Jemerin, J. (1990). Psychobiological differences in childhood stress response. I. Patterns of illness and susceptibility. *Journal of Developmental & Behavioral Pediatrics, 11*(2), 86.

Boyce, W., Quas, J., Alkon, A., Smider, N., Essex, M., & Kupfer, D. (2001). Autonomic reactivity and psychopathology in middle childhood. *The British Journal of Psychiatry, 179*(2), 144-150.

Boyle, J. (1997). Recurrent abdominal pain: An update. *Pediatrics in Review, 18*(9), 310-321.

Bruehl, S., Dengler-Crish, C., Smith, C., & Walker, L. (2010). Hypoalgesia related to elevated resting blood pressure is absent in adolescents and young adults with a history of functional abdominal pain. *Pain, 149*(1), 57-63.

Burke, P., Elliott, M., & Fleissner, R. (1999). Irritable bowel syndrome and recurrent abdominal pain: A comparative review. *Psychosomatics: Journal of Consultation Liaison Psychiatry*.

Burr, R., Heitkemper, M., Jarrett, M., & Cain, K. (2000). Comparison of autonomic nervous system indices based on abdominal pain reports in women with irritable bowel syndrome. *Biological Research for Nursing, 2*(2), 97-106.

Caceres, C., & Burns, J. (1997). Cardiovascular reactivity to psychological stress may enhance subsequent pain sensitivity. *Pain, 69*(3), 237-244.

Campo, J., Di Lorenzo, C., Chiappetta, L., Bridge, J., Colborn, D., Gartner Jr, J., et al. (2001). Adult outcomes of pediatric recurrent abdominal pain: Do they just grow out of it? *Pediatrics, 108*(1), e1.

Cannon, W. (1929). *Bodily changes in pain, hunger, fear and rage.* (2nd ed.). New York: Appleton-Century-Crofts.

Carroll, D., Ginty, A., Der, G., Hunt, K., Benzeval, M., & Phillips, A. (2012). Increased blood pressure reactions to acute mental stress are associated with 16-year cardiovascular disease mortality. *Psychophysiology, 49*(10), 1444-1448.

Carroll, D., Phillips, A., & Lovallo, W. (2012). The behavioral and health corollaries of blunted physiological reactions to acute psychological stress: Revising the reactivity hypothesis. In R. A. Wright & G. H. E. Gendolla (Eds.), *How motivation affects cardiovascular response: Mechanisms and applications* (pp. 243-263). Washington, DC: American Psychological Association.

Chang, L. (2011). The role of stress on physiological responses and clinical symptoms in irritable bowel syndrome. *Gastroenterology, 140*(3), 761.

Chang, L., Sundaresh, S., Elliott, J., Anton, P., Baldi, P., Licudine, A., et al. (2008). Dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis in irritable bowel syndrome. *Neurogastroenterology and Motility, 21*(2), 149-159.

Chatkoff, D., Maier, K., & Klein, C. (2010). Nonlinear associations between chronic stress and cardiovascular reactivity and recovery. *International Journal of Psychophysiology, 77*(2), 150-156.

Chida, Y., & Hamer, M. (2008). Chronic psychosocial factors and acute physiological responses to laboratory-induced stress in healthy populations: A quantitative review of 30 years of investigations. *Psychological Bulletin, 134*(6), 829-885.

Chitkara, D., van Tilburg, M., Blois-Martin, N., & Whitehead, W. (2008). Early life risk factors that contribute to irritable bowel syndrome in adults: A systematic review. *The American journal of gastroenterology, 103*(3), 765-774.

Claar, R., & Walker, L. (2006). Functional assessment of pediatric pain patients: Psychometric properties of the functional disability inventory. *Pain, 121*(1/2).

Clements, K., & Turpin, G. (2000). Life event exposure, physiological reactivity, and psychological strain. *Journal of Behavioral Medicine, 23*(1), 73-94.

Cohen, S., Hamrick, N., Rodriguez, M., Feldman, P., Rabin, B., & Manuck, S. (2002). Reactivity and vulnerability to stress-associated risk for upper respiratory illness. *Psychosomatic Medicine, 64*(2), 302.

Cole, D., & Maxwell, S. (2003). Testing mediational models with longitudinal data: Questions and tips in the use of structural equation modeling. *Journal of Abnormal Psychology, 112*(4), 558.

Compas, B., & Phares, V. (1991). Stress during childhood and adolescence: Sources of risk and vulnerability. In A. L. G. Mark E. Cummings, and Katherine H. Karraker (Ed.), *Life Span Developmental Psychology* (pp. 111-130). Hillsdale, NJ: Lawrence Erlbaum Associates, Inc.

Creed, F., Craig, T., & Farmer, R. (1988). Functional abdominal pain, psychiatric illness, and life events. *Gut, 29*(2), 235-242.

Davidson, R., Jackson, D., & Kalin, N. (2000). Emotion, plasticity, context, and regulation: Perspectives from affective neuroscience. *Psychological Bulletin, 126*(6), 890-909.

Dembroski, T., MacDougall, J., Slaats, S., Eliot, R., & Buell, J. (1981). Challenge-induced cardiovascular response as a predictor of minor illnesses. *Journal of Human Stress, 7*(4), 2-5.

Dickerson, S., & Kemeny, M. (2004). Acute stressors and cortisol responses: A theoretical integration and synthesis of laboratory research. *Psychological Bulletin, 130*, 355-391.

Dorn, L., Campo, J., Thato, S., Dahl, R., Lewin, D., Chandra, R., et al. (2003). Psychological comorbidity and stress reactivity in children and adolescents with recurrent abdominal pain and anxiety disorders. *Journal of the American Academy of Child and Adolescent Psychiatry, 42*(1), 66-75.

Drossman, D. (1998). Presidential address: Gastrointestinal illness and the biopsychosocial model. *Psychosomatic Medicine, 60*(3), 258-267.

Drossman, D. (2006). Rome III: The new criteria. *Chinese Journal of Digestive Diseases, 7*(4), 181-185.

Drossman, D., Creed, F., Olden, K., Svedlund, J., Toner, B., & Whitehead, W. (1999). Psychosocial aspects of the functional gastrointestinal disorders. *Gut, 45*(suppl 2), II25-II30.

Dufton, L., Dunn, M., Slosky, L., & Compas, B. (2011). Self-reported and laboratory-based responses to stress in children with recurrent pain and anxiety. *Journal of Pediatric Psychology, 36*(1), 95-105.

Dufton, L., Konik, B., Colletti, R., Stanger, C., Boyer, M., Morrow, S., et al. (2008). Effects of stress on pain threshold and tolerance in children with recurrent abdominal pain. *Pain, 136*(1), 38-43.

Ehlert, U., & Straub, R. (1998). Physiological and emotional response to psychological stressors in psychiatric and psychosomatic disorders. *Annals of the New York Academy of Sciences, 851*(1), 477-486.

El-Sheikh, M., Harger, J., & Whitson, S. (2001). Exposure to interparental conflict and children's adjustment and physical health: The moderating role of vagal tone. *Child Development, 72*(6), 1617-1636.

Ellis, B., Essex, M., & Boyce, W. (2005). Biological sensitivity to context: II. Empirical explorations of an evolutionary–developmental theory. *Development and Psychopathology, 17*(02), 303-328.

Elsenbruch, S., Lovallo, W., & Orr, W. (2001). Psychological and physiological responses to postprandial mental stress in women with the irritable bowel syndrome. *Psychosomatic Medicine, 63*(5), 805-813.

Evans, G., & Kim, P. (2007). Childhood poverty and health: Cumulative risk exposure and stress dysregulation. *Psychological Science, 18*(11), 953-957.

Evans, G., & Lepore, S. (1992). Conceptual and analytic issues in crowding research. *Journal of Environmental Psychology, 12*(2), 163-173.

Ewart, C., Jorgensen, R., Suchday, S., Chen, E., & Matthews, K. (2002). Measuring stress resilience and coping in vulnerable youth: The social competence interview. *Psychological assessment, 14*(3), 339-352.

Ewart, C., & Kolodner, K. (1991). Social competence interview for assessing physiological reactivity in adolescents. *Psychosomatic Medicine, 53*(3), 289.

Felitti, V., Anda, R., Nordenberg, D., Williamson, D., Spitz, A., Edwards, V., et al. (1998). Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. *American Journal of Preventive Medicine, 14*(4), 245-258.

Fichna, J., & Storr, M. (2012). Brain-gut interactions in IBS. *Frontiers in Pharmacology, 3*, 1-12.

Ford, M., Miller, P., Eastwood, J., & Eastwood, M. (1987). Life events, psychiatric illness and the irritable bowel syndrome. *Gut, 28*(2), 160-165.

Garber, J., Walker, L., & Zeman, J. (1991). Somatization symptoms in a community sample of children and adolescents: Further validation of the Children's Somatization Inventory. *Psychological assessment, 3*(4), 588-595.

Gerin, W., & Pickering, T. (1995). Association between delayed recovery of blood pressure after acute mental stress and parental history of hypertension. *Journal of Hypertension, 13*(6), 603.

Gieteling, M., Bierma-Zeinstra, S., Passchier, J., & Berger, M. (2008). Prognosis of chronic or recurrent abdominal pain in children. *Journal of Pediatric Gastroenterology and Nutrition, 47*(3), 316.

Greene, J., Walker, L., Hickson, G., & Thompson, J. (1985). Stressful life events and somatic complaints in adolescents. *Pediatrics, 75*(1), 19-22.

Gump, B., & Matthews, K. (1999). Do background stressors influence reactivity to and recovery from acute stressors? *Journal of Applied Social Psychology, 29*(3), 469-494.

Gump, B., Matthews, K., & Räikkönen, K. (1999). Modeling relationships among socioeconomic status, hostility, cardiovascular reactivity, and left ventricular mass in African American and White children. *Health Psychology, 18*, 140-150.

Gunnar, M., & Quevedo, K. (2007). The neurobiology of stress and development. *Annual Review of Psychology, 58*, 145-173.

Gwee, K., Leong, Y., Graham, C., McKendrick, M., Collins, S., Walters, S., et al. (1999). The role of psychological and biological factors in postinfective gut dysfunction. *Gut, 44*(3), 400-406.

Hamer, M., & Malan, L. (2010). Psychophysiological risk markers of cardiovascular disease. *Neuroscience and Biobehavioral Reviews, 35*(1), 76-83.

Heim, C., & Nemeroff, C. (2001). The role of childhood trauma in the neurobiology of mood and anxiety disorders: Preclinical and clinical studies. *Biological Psychiatry, 49*(12), 1023-1039.

Heim, C., Newport, D., Bonsall, R., Miller, A., & Nemeroff, C. (2003). Altered pituitary-adrenal axis responses to provocative challenge tests in adult survivors of childhood abuse. *Focus, 1*(3), 282.

Heim, C., Newport, D., Wagner, D., Wilcox, M., Miller, A., & Nemeroff, C. (2002). The role of early adverse experience and adulthood stress in the prediction of neuroendocrine stress reactivity in women: A multiple regression analysis. *Depression and Anxiety, 15*(3), 117-125.

Heitkemper, M., Burr, R., Jarrett, M., Hertig, V., Lustyk, M., & Bond, E. (1998). Evidence for autonomic nervous system imbalance in women with irritable bowel syndrome. *Digestive Diseases and Sciences, 43*(9), 2093-2098.

Heitkemper, M., Jarrett, M., Cain, K., Burr, R., Levy, R., Feld, A., et al. (2001). Autonomic nervous system function in women with irritable bowel syndrome. *Digestive Diseases and Sciences, 46*(6), 1276-1284.

Hotopf, M., & Carr, S. (1998). Why do children have chronic abdominal pain, and what happens to them when they grow up? Population based cohort study. *British Medical Journal, 316*(7139), 1196.

Hyams, J., & Hyman, P. (1998). Recurrent abdominal pain and the biopsychosocial model of medical practice. *Journal of Pediatrics, 133*(4), 473-478.

Hyams, J., Treem, W., Justinich, C., Davis, P., Shoup, M., & Burke, G. (1995). Characterization of symptoms in children with recurrent abdominal pain: Resemblance to irritable bowel syndrome. *Journal of Pediatric Gastroenterology and Nutrition, 20*(2), 209.

Hymowitz, G. (2011). Do previous life experiences and family history moderate gastrointestinal symptoms, somatic symptoms and stress in response to transient stressors? Unpublished doctoral dissertation. Stony Brook University, Stony Brook, NY.

Jemerin, J., & Boyce, W. (1990). Psychobiological differences in childhood stress response. II. Cardiovascular markers of vulnerability. *Journal of Developmental & Behavioral Pediatrics, 11*(3), 140.

Jones, M., Dilley, J., Drossman, D., & Crowell, M. (2005). Brain–gut connections in functional GI disorders: Anatomic and physiologic relationships. *Neurogastroenterology and Motility, 18*(2), 91-103.

Jørgensen, L., Bønløkke, L., & Christensen, N. (1986). Life strain, life events, and autonomic response to a psychological stressor in patients with chronic upper abdominal pain. *Scandinavian Journal of Gastroenterology, 21*(5), 605-613.

Jørgensen, L., Christiansen, P., Raundahl, U., Østgaard, S., Christensen, N., Fenger, M., et al. (1993). Autonomic nervous system function in patients with functional abdominal pain an experimental study. *Scandinavian Journal of Gastroenterology, 28*(1), 63-68.

Jorgensen, R., & Houston, B. (1986). Family history of hypertension, personality patterns, and cardiovascular reactivity to stress. *Psychosomatic Medicine, 48*(1), 102.

Juster, R., McEwen, B., & Lupien, S. (2009). Allostatic load biomarkers of chronic stress and impact on health and cognition. *Neuroscience & Biobehavioral Reviews, 35*(1), 2-16.

Kibler, J., & Ma, M. (2004). Depressive symptoms and cardiovascular reactivity to laboratory behavioral stress. *International Journal of Behavioral Medicine, 11*(2), 81-87.

Kirschbaum, C., Pirke, K., & Hellhammer, D. (1993). The 'Trier Social Stress Test'—a tool for investigating psychobiological stress responses in a laboratory setting. *Neuropsychobiology, 28*(1-2), 76-81.

Krantz, D., & Manuck, S. (1984). Acute psychophysiologic reactivity and risk of cardiovascular disease: a review and methodologic critique. *Psychological Bulletin, 96*(3), 435.

Kudielka, B., Buske-Kirschbaum, A., Hellhammer, D., & Kirschbaum, C. (2004). HPA axis responses to laboratory psychosocial stress in healthy elderly adults, younger adults, and children: Impact of age and gender. *Psychoneuroendocrinology, 29*(1), 83-98.

Lassner, J., Matthews, K., & Stoney, C. (1994). Are cardiovascular reactors to asocial stress also reactors to social stress? *Journal of Personality and Social Psychology, 66*(1), 69.

Lepore, S., Miles, H., & Levy, J. (1997). Relation of chronic and episodic stressors to psychological distress, reactivity, and health problems. *International Journal of Behavioral Medicine, 4*(1), 39-59.

Lercher, P. (1996). Environmental noise and health: An integrated research perspective. *Environment International, 22*(1), 117-129.

Levy, R., Olden, K., Naliboff, B., Bradley, L., Francisconi, C., Drossman, D., et al. (2006). Psychosocial aspects of the functional gastrointestinal disorders. *Gastroenterology-Orlando, 130*(5), 1447-1458.

Liakopoulou-Kairis, M., Alifieraki, T., Protagora, D., Korpa, T., Kondyli, K., Dimosthenous, E., et al. (2002). Recurrent abdominal pain and headache. *European Child and Adolescent Psychiatry, 11*(3), 115-122.

Locke, G., Weaver, A., Melton, L., & Talley, N. (2004). Psychosocial factors are linked to functional gastrointestinal disorders: A population based nested case-control study. *The American Journal of Gastroenterology, 99*(2), 350-357.

Low, C., Salomon, K., & Matthews, K. (2009). Chronic life stress, cardiovascular reactivity, and subclinical cardiovascular disease in adolescents. *Psychosomatic Medicine, 71*(9), 927-931.

Luecken, L., & Lemery, K. (2004). Early caregiving and physiological stress responses. *Clinical Psychology Review, 24*(2), 171-191.

Lupien, S., King, S., Meaney, M., & McEwen, B. (2001). Can poverty get under your skin? Basal cortisol levels and cognitive function in children from low and high socioeconomic status. *Development and Psychopathology, 13*(03), 653-676.

Manuck, S. (1994). Cardiovascular reactivity in cardiovascular disease:"Once more unto the breach". *International Journal of Behavioral Medicine, 1*(1), 4-31.

Matthews, K., Gump, B., Block, D., & Allen, M. (1997). Does background stress heighten or dampen children's cardiovascular responses to acute stress? *Psychosomatic Medicine, 59*(5), 488-496.

Matthews, K., Gump, B., & Owens, J. (2001). Chronic stress influences cardiovascular and neuroendocrine responses during acute stress and recovery, especially in men. *Health Psychology, 20*(6), 403-410.

Matthews, K., Salomon, K., Brady, S., & Allen, M. (2003). Cardiovascular reactivity to stress predicts future blood pressure in adolescence. *Psychosomatic Medicine, 65*(3), 410-415.

Matthews, K., & Stoney, C. (1988). Influences of sex and age on cardiovascular responses during stress. *Psychosomatic Medicine, 50*(1), 46-56.

Matthews, K., Woodall, K., & Allen, M. (1993). Cardiovascular reactivity to stress predicts future blood pressure status. *Hypertension, 22*(4), 479-485.

Maxwell, S., & Cole, D. (2007). Bias in cross-sectional analyses of longitudinal mediation. *Psychological Methods, 12*(1), 23.

Mayer, E. (2000). The neurobiology of stress and gastrointestinal disease. *Gut, 47*(6), 861.

Mayer, E., & Collins, S. (2002). Evolving pathophysiologic models of functional gastrointestinal disorders. *Gastroenterology, 122*(7), 2032-2048.

Mayer, E., Naliboff, B., Chang, L., & Coutinho, S. (2001). Stress and the gastrointestinal tract v. stress and irritable bowel syndrome. *American Journal of Physiology-Gastrointestinal and Liver Physiology, 280*(4), G519-G524.

Mazurak, N., Seredyuk, N., Sauer, H., Teufel, M., & Enck, P. (2012). Heart rate variability in the irritable bowel syndrome: A review of the literature. *Neurogastroenterology and Motility*.

McCubbin, H., & Patterson, J. (1987). Family Inventory of Life Events and Changes. In M. HI & P. JM (Eds.), *Family Assessment Inventories for Research and Practice* (pp. 80–108.). Madison: University of Wisconsin.

McEwen, B. (1998). Protective and damaging effects of stress mediators. *The New England Journal of Medicine, 338*(3), 171.

McEwen, B. (2000). The neurobiology of stress: From serendipity to clinical relevance. *Brain Research, 886*(1), 172-189.

McEwen, B. (2003). Early life influences on life-long patterns of behavior and health. *Mental Retardation and Developmental Disabilities Research Reviews, 9*(3), 149-154.

McEwen, B. (2004). Protection and damage from acute and chronic stress. *Annals of the New York Academy of Sciences, 1032*, 1–7.

McEwen, B., & Lasley, E. (2002). *The end of stress as we know it*. New York: Joseph Henry Press.

McEwen, B., & Wingfield, J. (2003). The concept of allostasis in biology and biomedicine. *Hormones and Behavior, 43*(1), 2-15.

McEwen, B., & Wingfield, J. (2010). What is in a name? Integrating homeostasis, allostasis and stress. *Hormones and behavior, 57*(2), 105-111.

McGrath, P., Goodman, J., Firestone, P., Shipman, R., & Peters, S. (1983). Recurrent abdominal pain: A psychogenic disorder? *Archives of Disease in Childhood, 58*(11), 888-890.

Miller, G., Chen, E., & Zhou, E. (2007). If it goes up, must it come down? Chronic stress and the hypothalamic-pituitary-adrenocortical axis in humans. *Psychological Bulletin, 133*(1), 25.

Mönnikes, H., Tebbe, J., Hildebrandt, M., Arck, P., Osmanoglou, E., Rose, M., et al. (2001). Role of stress in functional gastrointestinal disorders. Evidence for
stress-induced alterations in gastrointestinal motility and sensitivity. *Digestive Diseases, 19*(3), 201-211.

Mulvaney, S., Lambert, W., Garber, J., & Walker, L. (2006). Trajectories of symptoms and impairment for pediatric patients with functional abdominal pain: A 5-year longitudinal study. *Journal of the American Academy of Child & Adolescent Psychiatry, 45*(6), 737.

Musante, L., Treiber, F., Kapuku, G., Moore, D., Davis, H., & Strong, W. (2000). The effects of life events on cardiovascular reactivity to behavioral stressors as a function of socioeconomic status, ethnicity, and sex. *Psychosomatic Medicine, 62*(6), 760-767.

Nicholl, B., Halder, S., Macfarlane, G., Thompson, D., O'brien, S., Musleh, M., et al. (2008). Psychosocial risk markers for new onset irritable bowel syndrome–results of a large prospective population-based study. *Pain, 137*(1), 147.

Phillips, A. (2011). Blunted cardiovascular reactivity relates to depression, obesity, and self-reported health. *Biological Psychology, 86*(2), 106-113.

Phillips, A., Der, G., Shipton, D., & Benzeval, M. (2011). Prospective associations between cardiovascular reactions to acute psychological stress and change in physical disability in a large community sample. *International Journal of Psychophysiology, 81*(3), 332-337.

Porges, S. (2007). The polyvagal perspective. *Biological Psychology, 74*(2), 116-143.

Repetti, R., Taylor, S., & Seeman, T. (2002). Risky families: Family social environments and the mental and physical health of offspring. *Psychological Bulletin, 128*(2), 330-366.

Robinson, J., Alverez, J., & Dodge, J. (1990). Life events and family history in children with recurrent abdominal pain. *Journal of Psychosomatic Research, 34*(2), 171-181.

Ross, C. (2005). Childhood sexual abuse and psychosomatic symptoms in irritable bowel syndrome. *Journal of Child Sexual Abuse, 14*(1), 27-38.

Roy, M., Steptoe, A., & Kirschbaum, C. (1998). Life events and social support as moderators of individual differences in cardiovascular and cortisol reactivity. *Journal of Personality and Social Psychology, 75*(5), 1273.

Schwartz, A., Gerin, W., Davidson, K., Pickering, T., Brosschot, J., Thayer, J., et al. (2003). Toward a causal model of cardiovascular responses to stress and the development of cardiovascular disease. *Psychosomatic Medicine, 65*(1), 22.

Steptoe, A., & Marmot, M. (2005). Impaired cardiovascular recovery following stress predicts 3-year increases in blood pressure. *Journal of Hypertension, 23*(3), 529-536.

Talley, N., Fett, S., Zinsmeister, A., & Melton, L. (1994). Gastrointestinal tract symptoms and self-reported abuse: A population-based study. *Gastroenterology, 107*(4), 1040.

Taylor, S. (2010). Mechanisms linking early life stress to adult health outcomes. *Proceedings of the National Academy of Sciences, 107*(19), 8507.

Taylor, S., Repetti, R., & Seeman, T. (1997). Health psychology: What is an unhealthy environment and how does it get under the skin? *Annual Review of Psychology, 48*(1), 411-447.

Tillisch, K., Mayer, E., Labus, J., Stains, J., Chang, L., & Naliboff, B. (2005). Sex specific alterations in autonomic function among patients with irritable bowel syndrome. *Gut, 54*(10), 1396-1401.

Tougas, G. (2000). The autonomic nervous system in functional bowel disorders. *Gut, 47*(suppl 4), iv78-iv80.

Treiber, F., Kamarck, T., Schneiderman, N., Sheffield, D., Kapuku, G., & Taylor, T. (2003). Cardiovascular reactivity and development of preclinical and clinical disease states. *Psychosomatic Medicine, 65*(1), 46-62.

Treiber, F., Musante, L., Kapuku, G., Davis, C., Litaker, M., & Davis, H. (2001). Cardiovascular (CV) responsivity and recovery to acute stress and future CV functioning in youth with family histories of CV disease: A 4-year longitudinal study. *International Journal of Psychophysiology, 41*(1).

Videlock, E., Adeyemo, M., Licudine, A., Hirano, M., Ohning, G., Mayer, M., et al. (2009). Childhood trauma is associated with hypothalamic-pituitary-adrenal axis responsiveness in irritable bowel syndrome. *Gastroenterology, 137*(6), 1954-1962.

Walker, L., Baber, K., Garber, J., & Smith, C. (2008). A typology of pain coping strategies in pediatric patients with chronic abdominal pain. *Pain, 137*(2), 266-275.

Walker, L., Dengler-Crish, C., Rippel, S., & Bruehl, S. (2010). Functional abdominal pain in childhood and adolescence increases risk for chronic pain in adulthood. *Pain, 150*(3), 568-572.

Walker, L., Garber, J., & Greene, J. (1991). Somatization symptoms in pediatric abdominal pain patients: Relation to chronicity of abdominal pain and parent somatization. *Journal of Abnormal Child Psychology, 19*(4), 379-394.

Walker, L., Garber, J., & Greene, J. (1993). Psychosocial correlates of recurrent childhood pain: A comparison of pediatric patients with recurrent abdominal pain, organic illness, and psychiatric disorders. *Journal of Abnormal Psychology, 102*(2), 248.

Walker, L., Garber, J., & Greene, J. (1994). Somatic complaints in pediatric patients: A prospective study of the role of negative life events, child social and academic competence, and parental somatic symptoms. *Journal of Consulting and Clinical Psychology, 62*(6), 1213.

Walker, L., Garber, J., Smith, C., Van Slyke, D., & Claar, R. (2001). The relation of daily stressors to somatic and emotional symptoms in children with and without recurrent abdominal pain. *Journal of Consulting and Clinical Psychology, 69*(1), 85-91.

Walker, L., Garber, J., Van Slyke, D., & Greene, J. (1995). Long-term health outcomes in patients with recurrent abdominal pain. *Journal of Pediatric Psychology, 20*(2), 233-245.

Walker, L., & Greene, J. (1987). Negative life events, psychosocial resources, and psychophysiological symptoms in adolescents. *Journal of Clinical Child Psychology, 16*(1), 29-36.

Walker, L., & Greene, J. (1991a). The functional disability inventory: Measuring a neglected dimension of child health status. *Journal of Pediatric Psychology, 16*(1), 39.

Walker, L., & Greene, J. (1991b). Negative life events and symptom resolution in pediatric abdominal pain patients. *Journal of Pediatric Psychology, 16*(3), 341.

Walker, L., Guite, J., Duke, M., Barnard, J., & Greene, J. (1998). Recurrent abdominal pain: A potential precursor of irritable bowel syndrome in adolescents and young adults. *The Journal of Pediatrics, 132*(6), 1010.

Walker, L., Lipani, T., Greene, J., Caines, K., Stutts, J., Polk, D., et al. (2004). Recurrent abdominal pain: Symptom subtypes based on the Rome II criteria for pediatric functional gastrointestinal disorders. *Journal of Pediatric Gastroenterology and Nutrition, 38*(2), 187.

Walker, L., Sherman, A., Bruehl, S., Garber, J., & Smith, C. (2012). Functional abdominal pain patient subtypes in childhood predict functional gastrointestinal disorders with chronic pain and psychiatric comorbidities in adolescence and adulthood. *Pain, 153*(9), 1798-1806.

Walker, L., Smith, C., Garber, J., & Claar, R. (2005). Testing a model of pain appraisal and coping in children with chronic abdominal pain. *Health Psychology, 24*(4), 364-374.

Walker, L., Smith, C., Garber, J., & Van Slyke, D. (1997). Development and validation of the pain response inventory for children. *Psychological Assessment, 9*(4), 392.

Ware, J., & Sherbourne, C. (1992). The MOS 36-item short-form health survey (SF-36): I. Conceptual framework and item selection. *Medical Care, 30*(6), 473-483.

Waring, W., Chui, M., Japp, A., Nicol, E., & Ford, M. (2004). Autonomic cardiovascular responses are impaired in women with irritable bowel syndrome. *Journal of Clinical Gastroenterology, 38*(8), 658-663.

Wasserman, A., Whitington, P., & Rivara, F. (1988). Psychogenic basis for abdominal pain in children and adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry, 27*(2), 179-184.

Whitehead, W., Crowell, M., Robinson, J., Heller, B., & Schuster, M. (1992). Effects of stressful life events on bowel symptoms: Subjects with irritable bowel syndrome compared with subjects without bowel dysfunction. *British Medical Journal, 33*(6), 825.