

RECURRENT ABDOMINAL PAIN, ANXIETY, AND
RESPONSES TO STRESS IN CHILDREN AND ADOLESCENTS

By

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To my family, both blood-related and not, for your unending love and support.

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CHAPTER 1

INTRODUCTION

Recurrent and chronic somatic complaints, such as stomachaches, headaches, back pain, and fatigue, are common problems in childhood (Egger, Angold, & Costello, 1998). Though these types of symptoms are experienced by all children at some point in their lifetime, a subset of children have pain complaints that are frequent and severe enough to affect their everyday functioning. In fact, epidemiological studies suggest that 10 to 25% of children and adolescents report recurrent abdominal pain severe enough to disrupt school and social functioning (Alfven, 1993; Apley & Naish, 1958; Garber, Walker, & Zeman, 1991); 10 to 30 percent report weekly or frequent headaches (Egger, Angold, & Costello, 1998); and 5 to 20 percent complain of musculoskeletal pains (Abu-Arefeh & Russell, 1994; Kristjansdottir, 1997; Larsson, 1991). Oftentimes children with frequent pain complaints make repeated visits to their pediatrician's offices (Starfield, Katz, & Gabriel, 1984), go through expensive and sometimes invasive procedures (Walker, Garber, Van Slyke, & Greene, 1995), and place a heavy burden on the health care system (Walker, Garber, Van Slyke, & Greene, 1995).

Symptoms of anxiety and the diagnosis of anxiety disorders are also highly prevalent among children and adolescents. For example, in a community sample of 1,420 children and adolescents, Costello, Mustillo, Erkanli, Keeler, and Angold (2003) reported a 3-month prevalence rate of 2.4% and an estimated cumulative prevalence rate of 9.9% of any anxiety disorder by the age of 16-years-old. Similarly, Lewinsohn, Hopps,

Roberts, Seeley, and Andrews (1993), in a sample of over 1,500 adolescents, reported a lifetime prevalence rate of 8-9% for any anxiety disorder. Although mild anxiety problems are often short-lived, childhood anxiety disorders are often chronic, interfering substantially with children's adaptive functioning and persisting into adulthood (Keller et al., 1992 ; Ollendick, Hagopian, & King, 1998). Indeed, many adult anxiety disorders appear to have their onset in childhood (Burke, Burke, Regier, & Rae, 1990; Ost, 1987). Thus, there is a clear need for improved understanding of the factors contributing to the development, persistence and remission of such problems.

One potential avenue for research is the examination of comorbid somatic complaints in children with anxiety. The comorbidity between chronic pain and anxiety disorders in childhood is high (e.g., Last, 1991), and as such many children with anxiety who complain also of chronic or recurrent pain, such as abdominal pain, may present at their pediatrician's clinic for treatment (Campo et al., 2004; Campo, Comer, Jansen-McWilliams, Gardner, & Kelleher, 2002). Therefore, understanding the association between pain and anxiety may be particularly useful in discerning diagnosis and developing treatment plans.

The association between recurrent or chronic pain and anxiety in children is important for several reasons. First, there is much evidence showing a strong association between physical and psychological problems in children and adolescents. For example, in a large population-based community sample, stomachaches, headaches, and musculoskeletal pains were strongly associated with anxiety, depression, and behavioral disorders in children and adolescents age 9 to 16-years-old (Egger, Costello, Erkanli, & Angold, 1999). Second, physical symptoms are often part of the criteria for a

psychological disorder, and as such they are intrinsically linked. For example, “repeated complaints of physical symptoms (such as headaches, stomachaches, nausea, or vomiting) when separation from major attachment figures occurs or is anticipated” is one of the core symptoms of Separation Anxiety Disorder as defined by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV, American Psychiatric Association, 1994). Third, pain symptoms may exacerbate or contribute to psychological symptoms, and vice versa. For example, a child with recurrent stomachaches may become fearful or anxious in situations in which she may be far from a restroom, and as a result she may refuse to leave home to attend school or other social functions. Her avoidance of social situations may, in turn, increase her anxiety when she is anticipating or forced to engage in activities outside the home, which may also then exacerbate her gastrointestinal symptoms.

A challenge for health care providers when working with families of children with chronic pain and anxiety is understanding the variety of factors that influence physical and psychological health and illness in children. Particularly in cases where a clear organic cause of children’s pain is not found, other factors that influence the course and outcome of the illness must be examined in order to inform treatment. As such, healthcare professionals are increasingly considering biopsychosocial (BPS) models of health and illness, models that encompass not only the disease of the patient, but also the context in which the disease occurs (Gatchel, Peng, Peters, Fuchs, & Turk, 2007; Hyams & Hyman, 1998). In BPS models, the concept of wellness is particularly stressed, where “good health” is not only freedom from disease, but is also accompanied by good quality of life and strong interpersonal relationships. As Engel (1977, p.132) states, “To provide a basis for understanding the determinants of disease and arriving at rational treatments

and patterns of health care, a medical model must also take into account the patient, the social context in which he lives and the complementary system devised by society to deal with the disruptive effects of illness, that is, the physician role and the health care system. This requires a biopsychosocial model.”

Since Engle first elucidated these ideas, research has shown that psychosocial factors have direct physiologic and pathologic consequences for physical disease and vice versa (e.g., Hyams & Hyman, 1998). An illness may arise from any one or a combination of factors including organic disease, functional disorder, psychological disorder, exposure, reactivity to and recovery from stress, emotional distress, or a patient’s or caregiver’s interpretation of symptoms. Attention to each of these areas and their combinations expands the potential for accurate diagnosis and treatment of illness.

This study examines some of the various psychological and psychophysiological factors and processes that influence a common pain condition in children, recurrent abdominal pain (RAP). Because RAP often has no known organic cause, psychosocial factors and reactivity to stress may play a key role in the development and maintenance of this condition. Further, anxiety symptoms and disorders are highly comorbid with RAP in children. A central hypothesis of this study is that anxiety and reactivity to stressful events are critical psychological factors in pediatric RAP and anxiety disorders. Therefore, this study examines potential underlying mechanisms that are either common to or discriminate between RAP and anxiety in children.

Before going on to describe the current study, I first provide an overview of research detailing the association between RAP and anxiety in children. Then I explore the potential underlying mechanisms that may contribute to both RAP and anxiety

symptoms and disorders. These mechanisms include temperament, reactivity to stress, and coping. Lastly, I state the hypotheses and describe the methods and results of the current study that examines potential underlying mechanisms that are either common to or discriminate between RAP and anxiety in children.

Recurrent Abdominal Pain

Recurrent abdominal pain is the most common recurrent pain complaint of childhood (McGrath, 1990). RAP is characterized as paroxysmal (i.e., sudden), periumbilical (i.e., occurring adjacent to the navel), nonradiating (i.e., does not extend outside of the stomach region), and episodic pain that significantly interferes with normal functioning (Colletti, 1998). The pain must occur at least once a month for at least 3 months in order to meet traditional criteria (Apley, 1975). Epidemiological studies suggest that RAP affects 8 to 25% of school-age children ages 9-12 years old (Alfven, 1993; Garber, Walker, & Zeman, 1991; Hyams, Burke, Davis, Rzepski, & Andrulonis, 1996), and is more prevalent among girls (Apley, 1975; Colletti, 1998).

Children with RAP report increased restrictions in daily activities due to their pain (Roth-Isigkeit, Raspe, Stoven, Thyen, & Schmucker, 2003). Further, children with RAP commonly report sleep disturbances, eating difficulties or appetite changes, and self-reported restrictions. As compared to children with back pain, for example, children with RAP miss significantly more days of school. Additionally, children with abdominal pain report that they are not able to spend time with their friends or participate in sports or hobbies because of their pain (Roth-Isigkeit, Thyen, Stoven, Scharzenberger, & Schmucker, 2005).

RAP accounts for 2% to 4% of all pediatric outpatient office visits (Starfield, Katz, & Gabriel, 1984), and many children with RAP go through potentially dangerous or unnecessary hospitalizations, tests and procedures, thus placing a heavy burden on the medical community. Medical evaluations reveal organic disease in fewer than 5% of children evaluated for RAP in primary care settings (Stickler & Murphy, 1979). Nonetheless, one-third to one-half of children with RAP continue to complain of abdominal pain and related symptoms after they reach adulthood (Walker, Garber, Van Slyke, & Greene, 1995).

Because in most cases no organic cause can be found to explain the child's pain, RAP is often defined as "functional." Functional gastrointestinal disorders are defined as conditions in which a "variable combination of chronic or recurrent gastrointestinal symptoms is present in the absence of any readily identifiable structural or biochemical abnormality" (Thompson et al., 1999). This definition of RAP lends itself to a biopsychosocial approach to understanding this potentially debilitating condition. Biological factors in RAP include physical pathology or physical changes in the stomach and intestines that generate nociceptive signals transmitted to the brain. Psychological factors include beliefs about pain developed from prior pain and illness experiences, coping responses to the pain, and concurrent psychological symptoms that may affect coping, beliefs, and attention (Compas et al., 2006). Additionally, attention to pain sensations, appraisal of pain sensation, including interpretation of its meaning and one's ability to cope with it, temperament, and emotional states are other psychological factors that are involved in the modulation of nociceptive signals from the gut (Compas & Boyer, 2001). Socio-contextual factors include exposure to chronic or recurrent stressors,

behavior of significant others (e.g., caregivers, teachers, and peers) which may shape children's pain responses and beliefs by encouraging healthy and active responses to pain or adoption of a sick role, and by providing children with a model for pain behavior when responding to their own pain (Walker, Garber, & Greene, 1991). Thus, the BPS view of RAP integrates multiple components that are relevant to the experience of pain and pain-related disability.

Anxiety in Children

Anxiety problems and disorders are among the most common forms of emotional disturbance in childhood and adolescence (Anderson, 1994; Hagopian & Ollendick, 1997) with estimates of overall population prevalence ranging from 12% to 17.3% (Anderson, Williams, McGee, & Silva, 1987; Kashani, Orvaschel, Rosenberg, & Reid, 1989). When only confirmed disorders or those meeting minimal requirements for impairment are considered, however, the prevalence rate lowers to 2.4% to 8.7% (Anderson, 1994).

The Diagnostic and Statistical Manual of Mental Disorders, Third Edition (DSM-III; American Psychiatric Association, 1980) introduced three anxiety disorders that were specific to children: Separation Anxiety Disorder, Overanxious Disorder, and Avoidant Disorder. Additionally, the DSM-III introduced a wide range of adult anxiety disorders that were also applicable to children. As defined in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV; American Psychiatric Association, 1994), anxiety disorders include Specific Phobia, Social Phobia, Panic Disorder with and without Agoraphobia, Generalized Anxiety Disorder, Obsessive-Compulsive Disorder,

and Posttraumatic Stress Disorder. With the publication of DSM-IV, the childhood anxiety disorder categories of OAD and avoidant disorder were subsumed, respectively, under the categories of GAD and Social Phobia. Overanxious disorder was dropped from the DSM-IV, largely because studies consistently failed to support its validity (Beidel, 1991).

A biopsychosocial model of childhood anxiety includes psychological characteristics, physiological correlates of anxiety (including temperament, psychophysiological functioning, and autonomic nervous system functioning), and family and other environmental features that may contribute to the onset or maintenance of an anxiety disorder. Psychological features of anxiety in children include worry and cognitive biases and distortions towards threat. For example, preliminary evidence of threat-related information-processing biases among children with behavioral inhibition when they were followed-up at 13 years of age (Schwartz, Snidman, & Kagan, 1996) suggests that such biases may mediate the risk for anxiety disorders. In addition, significant psychological impairment, such as high trait anxiety, lower self-reported cognitive competence, and low self-esteem have been found in children with anxiety disorders (Beidel, 1991; Last, 1991; Messner & Beidel, 1994). Temperamental features, such as anxiety sensitivity (Chorpita & Lilianfeld, 1999), behavioral inhibition (discussed below; Kagan, Reznick, & Snidman, 1988), and fearfulness, have also been shown to put children at risk for anxiety disorders (Merikangas, Avenevoli, Dierker, & Grillon, 1999). Physiological features of anxiety include an increased startle response, greater galvanic skin response (GSR), and lower sensitivity to orthostatic change (Merikangas, 1999). Finally, family characteristics also contribute to a vulnerability towards anxiety in

children. For example, all major subtypes of anxiety disorders have been shown to aggregate in families (Kendler, Neale, Kessler, Heath, & Eaves, 1993; Skre, Onstad, Torgersen, Lygren, & Kringlen, 1993; Weissman, 1993). Parents high in anxiety have been shown to be over-involved in their parenting style (Hudson & Rapee, 2001), which may contribute to the child's overall lowered level of self-competence and increase their level of anxiety particularly when faced with new cognitive or social tasks. Thus, just as in RAP, the BPS view of anxiety also integrates the various features that contribute to the onset and maintenance of anxiety disorders in children.

Psychological Comorbidity of Symptoms and Diagnoses of Anxiety in Children with RAP

In descriptions of clinical cases, children with RAP are often described as “anxious, high strung, excitable, fussy, timid and apprehensive” (Apley & Naish, 1958, p. 168). A “typical” child with RAP is seen as an “anxious, driven child who seeks the approval of adults” (Scharff, 1997, p. p.151). These clinical observations and descriptions have received empirical support as many studies have shown an association between RAP and symptoms of psychopathology, particularly anxiety disorders, in children and adolescents (e.g., Blanchard & Scharff, 2002). A recent meta-analysis examined sixteen studies that assessed levels of anxiety and other internalizing symptoms in children and adolescents with RAP using self- and parent-report questionnaires (Dufton & Compas, 2008). These authors found that, when compared to healthy controls, children with RAP reported higher levels of anxiety symptoms across several different measures with effect sizes ranging from moderate to large. When compared to children with an organic cause for their stomach pain, 3 studies (Garber, Zeman, &

Walker, 1990; Walker, Garber, & Greene, 1993; Walker & Greene, 1989) found a moderately higher level of anxiety in children with RAP (mean Hedges $g = .58$). This meta-analysis provides evidence that anxiety in particular appears to be associated with RAP in children and adolescents (Dufton & Compas).

In addition to the assessment of self-, parent-, and teacher-reports of symptoms of psychopathology through questionnaires, several studies have conducted psychiatric diagnostic interviews with children and their parents in order to assess psychopathology in children with RAP. The most reliable diagnoses are made with structured or semi-structured interviews; the semi-structured format of some interview protocols allows the clinician or researcher the flexibility to pursue specific questions in greater detail when deemed necessary (March & Albano, 1996). Clinical interviews are the only method to derive diagnoses based on criteria specified by the DSM (American Psychiatric Association, 1994), and as such are the best means to determine whether the increased levels of anxiety symptoms found in children with RAP meet diagnostic criteria for an anxiety disorder.

In the earliest reported study using structured diagnostic interviews, Garber et al. (1990) examined the prevalence of psychiatric diagnoses in children with RAP. Using the Schedule for Affective Disorders and Schizophrenia for School-Aged Children (K-SADS) (Puig-Antich & Chambers, 1978), Garber et al. compared children meeting criteria for RAP ($n = 13$) with 3 other groups: children who had an organic cause to their abdominal pain (such as damage, inflammation, structural change, or abnormal growth) ($n = 11$); a psychiatric comparison group consisting of patients who presented to an outpatient psychiatric clinic for evaluation for emotional problems ($n = 19$); and a

matched healthy comparison group (n = 16). Garber et al. identified an anxiety disorder in 11 (85%) of 13 children with RAP. Of those meeting criteria for anxiety disorders, overanxious disorder was found in 9 (69%) children and separation anxiety disorder was found in 2 (15%) children. Interestingly, anxiety disorders were also frequently diagnosed among the children with an organic diagnosis for their abdominal pain. In the organic group, 5 (45%) children met criteria for separation anxiety disorder and 8 (73%) met criteria for overanxious disorder. The rates of disorders in both groups of children with abdominal pain (RAP and organic) were significantly higher than that found among healthy controls, and were not significantly different from that found in the psychiatric group. That is to say, rates of psychiatric disorders in the RAP group were similar to those found in a group of children referred for psychiatric services.

Dorn et al. (2003) compared children meeting criteria for RAP (n = 14) with children meeting criteria for an anxiety disorder (n = 14) and matched healthy controls (n = 14) using the K-SADS-PL. These researchers found an anxiety disorder in 9 (64%) children with RAP as compared to 14 (100%) of children in the anxiety disorder group and 0 (0%) of healthy controls. The most common diagnoses in children with RAP in this sample were GAD and separation anxiety disorder (56% and 44% of children with RAP who met criteria for an anxiety disorder, respectively).

More recently, Campo et al. (2004) examined the prevalence of psychiatric disorders in children and adolescents currently meeting criteria for RAP. Forty-two children with RAP and 38 matched healthy controls and their parents were interviewed using the Schedule for Affective Disorders and Schizophrenia for School Age Children, Present and Lifetime Version (K-SADS-PL; Kaufman et al., 1997). Campo et al. found

that a current anxiety disorder was identified in 33 (79%) of children with RAP, as compared to 4 (11%) controls. In the RAP group, separation anxiety disorder was found in 18 (43%) patients, generalized anxiety disorder found in 13 (31%) patients, and social phobia in 9 (21%) patients.

Data from these three studies show that the most common anxiety disorder diagnoses in children with RAP are Separation Anxiety Disorder, Generalized Anxiety Disorder, and DSM-III-R-based criteria for Overanxious Disorder. Since these disorders include somatic symptoms as part of their criteria, it is possible that the rates of these diagnoses are inflated and potentially confounded with symptoms of RAP. For example, criteria for Generalized Anxiety Disorder and Overanxious Disorder include frequent stomachaches or headaches, feeling “uptight or tense” a lot, and restlessness. Additionally, Separation Anxiety Disorder includes “repeated occurrence of physical symptoms (nausea, stomachache, headache, vomiting, etc.) on occasions that involve separation from a major attachment figure, such as leaving home to go to school” as part of its criteria (APA, 1994). Garber et al. (1990) addressed this concern by calculating the percentage of children who would have met the anxiety disorders criteria even if the somatic symptoms were excluded. Eighty-one percent of the children with RAP still met criteria for an anxiety disorder diagnosis even with their somatic symptoms excluded. Therefore, in at least one study, the presence of an anxiety disorder is not accounted for by somatic complaints only.

The National Comorbidity Replication Study places the lifetime prevalence of any anxiety disorder in the general adult population at 18.1% (Kessler, Chiu, Demler, & Walters, 2005). In children, the true prevalence of anxiety disorders is less well

established, but has been reported to be at approximately 8-10% (e.g., Costello et al., 2003; Fergusson, Horwood, & Lynskey, 1993; Lewisohn et al., 1993). Therefore, the lifetime prevalence of anxiety disorders in the samples of children with RAP reviewed here is much higher than would be expected in the general population and higher than in healthy control samples included in these studies. Anxiety appears to be a major concern in this population; children with RAP not only have higher than average symptoms of anxiety (as reviewed in the previous section), but their levels of anxiety are severe enough to qualify for a diagnosis.

Somatic Symptoms and Complaints in Children and Adolescents with Anxiety Disorders

The relationship between RAP and anxiety can be further examined in studies that have examined the rates of somatic symptoms, especially stomach pain, among children with anxiety disorders. These studies complement research that has documented anxiety symptoms and disorders among children with RAP, as the rates of co-occurrence of symptoms may differ as a result of bidirectional patterns of comorbidity. That is, the rates of stomach pain among children with anxiety disorders may differ from the rates of anxiety symptoms and disorders among children with RAP. A more complete picture of the relations between anxiety and RAP can be gained from viewing these associations from both directions. If children with a psychiatric diagnosis also have somatic symptoms in addition to psychological problems, important clues about the correlation between somatic symptoms and psychopathology may be determined. Children with RAP may be an interesting example of bidirectional comorbidity. That is, it could be that most or all children with anxiety have RAP, most or all children with RAP have anxiety,

or that there may be only a subset of children with both RAP and anxiety.

Several clinical studies have shown that children with anxiety disorders and depressive disorders report high rates of stomachaches and other somatic symptoms (Ginsburg, Riddle, & Davies, 2006; Last, 1991; Masi, Favilla, Millepiedi, & Mucci, 2000). Though a complete review of this literature is beyond the scope of this paper due to the vast nature of this literature, this section aims to briefly review studies that assessed somatic symptoms in children with anxiety or depression.

Anxiety disorders and stomach pain.

Several studies using clinically-referred samples have shown that children with anxiety disorders report high rates of stomachaches and other somatic symptoms (e.g., Beidel, Christ, & Long, 1991; Bernstein, Garfinkel, & Hoberman, 1989; Ginsburg et al., 2006; Last, 1991; Livingston, Taylor, & Crawford, 1988; McCauley, Carlson, & Calderon, 1991). For example, Ginsburg et al. (2006) evaluated the prevalence of somatic symptoms in children and adolescents with anxiety disorders. This 5-site study enrolled 120 children who met criteria for a current DSM-IV diagnosis of social phobia, separation anxiety disorder and/or generalized anxiety disorder. Ninety-six percent of the total sample reported at least one somatic symptom, and an average of six somatic symptoms were reported per child. Stomachaches were found in 70% of their sample.

Last (1991) examined somatic complaints in an outpatient sample of children with anxiety disorders and found that this sample endorsed high rates of somatic symptoms. Children in this study were classified as “somatic” (60%, n = 95) or “nonsomatic” (40%, n = 63) based on their responses to a semi-structured diagnostic interview (i.e., K-SADS).

Children classified as “somatic” and who met criteria for an anxiety disorder tended to be older than children who were anxiety-disordered and “nonsomatic.” Further, adolescents with anxiety disorders who reported more somatic complaints were more likely to demonstrate school refusal (Last, 1991).

In a study by Livingston, Taylor and Crawford (1988), somatic complaints in child psychiatric inpatients were associated with anxiety disorders, major depression, and psychosis. These researchers recruited 95 psychiatrically hospitalized children and interviewed them using the Diagnostic Interview for Children and Adolescents (DICA; Reich & Welner, 1990). The DICA provides data not only about psychiatric symptoms and diagnoses, but also asks questions about somatic symptoms that are medically unexplained and associated with impairment (i.e., went to the doctor, missed school, or took medication other than aspirin) during the period when symptoms were present. Abdominal pain was reported by 27.4% of the sample and was associated with separation anxiety disorder, psychosis, and depression (as classified as “definite” or “possible” current major depressive disorder). Livingstone, Taylor and Crawford note, however, that their sample may have been skewed as children may over-report emotional and somatic symptoms that may not be clinically significant.

Bernstein et al. (1997) found that children and adolescents with diagnoses of anxiety or depression commonly endorsed autonomic and gastrointestinal problems. Bernstein et al. recruited 44 adolescents 12 to 19 years of age with a diagnosis of anxiety or depression in an ongoing treatment study of school refusal. Gastrointestinal pain, rated by a clinician as moderate to severe, was found in 34.1% of their sample. Separation anxiety in particular was predicted by both the presence of gastrointestinal

symptoms and the absence of cardiovascular symptoms. Finally, symptoms of anxiety and depression significantly predicted the severity of somatic symptoms and school refusal (Bernstein et al., 1997).

The most comprehensive study examining somatic complaints and psychopathology in children and adolescents comes from data from a child psychiatric epidemiologic study of 4,500 children and adolescents in western North Carolina as part of the Great Smoke Mountains Study (Egger, Costello, Erkanli, & Angold, 1999). Egger et al. evaluated 4 waves of interviews with 9- to 16-year olds from this sample. The overall point prevalence of stomachaches was 2.8%. Significantly more girls reported stomachaches than did boys (3.8% versus 1.9%). Importantly, 60% of girls with an anxiety disorder reported one or more somatic complaints, compared with 12.1% of girls without an anxiety disorder. Stomachaches and headaches together were associated with among girls with an anxiety disorder. Stomachaches were associated with oppositional defiant disorder and ADHD, but not anxiety disorders, in boys. It is striking that Egger et al. found the point-prevalence rate of stomachaches in their sample to be only 2.8%, given that other community-based studies assessing the prevalence of RAP in the population to be between 8 to 25% (Alfven, 1993; Garber, Walker & Zeman, 1991; Hyams et al., 1996). Egger et al. note, however, that they assessed whether the child endorsed frequent stomachaches with only one item, and as such measurement issues may have underestimated the overall rate of abdominal pain in their sample.

Specific anxiety disorder diagnoses and somatic symptoms.

Few studies have evaluated the relationship between specific anxiety disorders and associated somatic symptoms (Bernstein, 1997). However, there is some evidence that somatic complaints are more often associated with separation anxiety disorder (SAD), generalized anxiety disorder (GAD), and panic disorder (PD) (Last, 1991; Livingston et al., 1988).

Ginsburg et al. (2006) found that children with SAD reported significantly more stomachaches, restlessness, and heart palpitations as compared to children without separation anxiety disorder. Interestingly, these somatic symptoms are not part of the diagnostic criteria for SAD. Also, children with GAD reported more stomachaches, restlessness, and chills or hot flashes than children without GAD.

Bernstein et al. (1997) found that among children with anxiety disorders, SAD and avoidant disorder were associated with specific patterns of somatic complaints such as stomachaches, headaches and musculoskeletal pains. A more detailed examination revealed that SAD was predicted by the presence of GI symptoms. In fact, adolescents who endorsed severe gastrointestinal symptoms compared to those reporting no gastrointestinal symptoms were 8.4 times more likely to have SAD.

Another study showing the relationship between specific anxiety disorders and somatic symptoms comes from Last et al. (1991). These researchers also found that somatic complaints were significantly more likely to be associated with SAD and PD. Livingston et al. (1998) had similar findings; that is, children with SAD also reported significantly more gastrointestinal symptoms than children with a different anxiety diagnosis. Finally, Egger et al. (1999) also reported that stomachaches and headaches

were significantly associated with GAD and that stomachaches and musculoskeletal pains were associated with separation anxiety disorder.

*Influences of Temperament and Physiological Responses to Stress
on the Development and Course of Recurrent Abdominal Pain*

Research establishing a relationship between RAP and other somatic symptoms with symptoms and diagnoses of anxiety raises questions about the processes or mechanisms that may account for these associations. There may be psychological and/or biological characteristics of children as well as factors in the social environment that may contribute to the association of RAP with anxiety. Foremost among such factors are children's temperament and the ways that children respond to and cope with stress. In this section several key temperamental and physiological factors that have been identified in children with RAP are reviewed. Temperamental characteristics are explored followed by responses to stress, including stress reactivity and coping, and properties of the autonomic nervous system that are implicated in RAP. Finally, the link between these biological substrates and anxiety and RAP will be considered.

Temperament: Implications for Anxiety and Pain in Children with RAP

Temperament is broadly defined as individual differences in behavior, mood, reactivity, and regulation which appear early in life, are consistent over time and across situations, and are presumed to have an underlying biological basis (Rothbart & Bates, 1998; Shiner, 1998). An underlying assumption of most conceptualizations is that

temperamental characteristics are genetic in origin but may be modified by experience. Certain temperamental tendencies or characteristics explain in part how individuals exposed to high levels of stress or uncertainty may do well while some individuals will experience difficulty after exposure to even very low levels of stress.

“Behavioral inhibition to the unfamiliar” is a temperamental tendency to become physiologically aroused and behaviorally restrained in the face of novelty (Kagan, Reznick, & Snidman, 1988; Kagan, Snidman, & Peterson, 2000). Inhibited children are typically shy as toddlers, quiet and withdrawn with unfamiliar people during the preschool years, and reticent with peers in middle childhood. This temperamental style is categorized by long latencies to approach novel stimuli, high frequency of negative affect, and fear of unfamiliar social situations (Kagan, Snidman, & Peterson, 2000). Behavioral inhibition in infancy has been found to be associated with increased risk for childhood anxiety disorders (Biederman et al., 1993; Biederman et al., 1990; Hirshfeld et al., 1992).

Children with RAP have been found to display many temperamental features found in behaviorally inhibited children. For example, in his seminal work Apley (1975) described his sample of children with RAP as “anxious, high strung, excitable, fussy, timid, and apprehensive.” Campo et al. (2004) was the first study to systematically document higher levels of anxious or inhibited temperament in children with RAP compared with pain-free control subjects. Children with RAP were rated as significantly higher in levels of temperamental Harm Avoidance than control subjects on the Junior Temperament and Character Inventory completed by mothers (Luby, Svrakic, McCallum, Przybeck, & Cloninger, 1999). Harm avoidance, or the tendency to respond intensely to

aversive stimuli and to avoid punishment, novelty, and non-reward passively, has been associated with behavioral inhibition. In addition to being related to behavioral inhibition, harm avoidance is also related to pessimistic worry, fear of uncertainty, a tendency to respond to environmental challenge at lower thresholds, vulnerability to anxiety and depressive disorders, and, interestingly, functional gastrointestinal symptoms in adults (Andrews, 1996; Talley, Boyce, & Jones, 1998; Watson & Pennebaker, 1989). These temperamental characteristics may lay the groundwork for the development of RAP as children mature and are exposed to increasing numbers of life events and stressors. For example, the child's tendency to worry and shy away from potential threats may increase her overall level of anxiety and concurrent sympathetic arousal, and ultimately diminish her ability to cope (see "Responses to Stress, Coping, RAP and Anxiety" below).

Differences in temperament have been associated with more general differences in biobehavioral reactivity to stress (Boyce, Barr, & Zeltzer, 1992). For example, behavioral inhibition has been associated with a number of psychophysiological correlates, including a high and stable resting heart rate (Kagan, Reznick, & Snidman, 1988), elevated basal salivary cortisol levels (Kagan, Reznick, & Snidman, 1988), heightened baseline startle responses (Snidman, Kagan, Roirdan, & Shannon, 1995), and greater relative resting right vs. left frontal EEG activity (Fox et al., 1995). Many of these psychophysiological responses to stress are also found in anxious children, adolescents, and adults (e.g., Grillon, Ameli, Merikangas, Woods, & Davis, 1993; Thayer, Friedman, & Borkovec, 1996).

Given that behavioral inhibition may be a temperamental precursor to RAP, in

addition to being associated with both RAP and anxiety, children with RAP may also display these same psychophysiological correlates. Dorn et al. (2003) compared children with RAP with children with well children as well as children with anxiety disorders on several physiological variables in response to a stress task (Trier Social Stress Test; Buske-Kirshbaum et al., 1997). They examined heart rate, systolic and diastolic blood pressure, and cortisol levels. Dorn et al. found that children with RAP and children with anxiety had a more robust response to the stress task on measures of heart rate and systolic blood pressure than healthy controls, and that, in general, the physiological response of the RAP group was indistinguishable from that of the anxious group. Temperamentally-based biological predispositions that may contribute to both RAP and anxiety might account for Dorn et al.'s findings.

Though little research has been done examining temperament in children with RAP, it remains a promising area of research that may contribute to our overall understanding of this condition, which will be further explored below.

Responses to Stress in Children with RAP

Temperament is hypothesized to indicate a certain innate predisposition to respond to the environment in a particular manner. Connected with temperament is the way in which children respond to and recover from stress (Compas, 1987; Compas, Connor-Smith, & Jaser, 2004). Physiological variables associated with temperament, such as diurnal variation in circulatory levels of cortisol or baseline resting heart rate, may raise or lower the threshold for a child to respond to stress. That is, for some children with a behaviorally inhibited or anxious temperament, it may take only a small

amount of stress to elicit a biobehavioral response to the stressor whereas for others it may require large or repeated amounts of stress to elicit the same reaction. Because children with RAP may already have a predisposition to be behaviorally inhibited, their response to stress may be exaggerated and recovery delayed. Therefore, one key component to understanding the development and maintenance of RAP in children may be patterns of both controlled (coping) and automatic responses to stress.

Stress is implicated in RAP at least two ways (Compas & Boyer, 2001). First, acute and chronic stress can contribute to the onset and course of RAP. In a seminal study of the relation between stress and episodes of pain in children with RAP, Walker et al. (2001) used daily assessment by phone interview to examine the relation of minor daily stressors to somatic and emotional symptoms. They found that children with RAP reported more daily stressors than well children, and that daily stressors more strongly predicted somatic symptoms in children with RAP than controls, suggesting that children with RAP are more likely to respond to stress with somatic symptoms than are healthy children. Further, Dufton, Konik, Colletti, Stanger, Boyer, Morrow & Compas (in press) found that mild laboratory stressors decreased pain tolerance in children with RAP. The second role played by stress in children with RAP is that the experience of pain itself constitutes a significant stressor (Compas & Boyer, 2001). Pain is a signal of threat to the health and well being of the child, and it is a noxious internal state that may challenge or exceed the child's adaptive capacities and thus make it difficult for them to cope (see “Stress and Coping in RAP and Anxiety” below).

Stress Reactivity and Recovery

Behavioral inhibition influences the processes governing stress reactivity and recovery, both of which are important to anxiety and pain (Compas, Connor-Smith, Saltzman, Thomsen, & Wadsworth, 2001). How individuals react to and recover from acute and chronic stress may be indicative of healthy or maladaptive psychological and somatic functioning. For example, as noted above, exposure to stress has been shown to predict pain episodes in children with RAP (Walker et al., 2001). Additionally, in adults a decreased ability to recover from stress has been found in women with Irritable Bowel Syndrome (Heitkemper et al., 1998).

The sympathetic nervous system (SNS) and parasympathetic nervous system (PNS) branches of the autonomic nervous system govern individuals' automatic responses to stress. The SNS quickly prepares the body to respond to stress by increasing the heart rate and blood pressure, dilating the pupils, triggering the release of epinephrine and norepinephrine, and slowing down digestive and reproductive processes. Once the stress response is activated, soon thereafter the processes responsible for stress recovery begin. The PNS controls the body's ability to recover from stress by slowing the heart rate, decreasing the blood pressure, and restoring regenerative processes, including digestion. Individual differences in stress reactivity and recovery may be found in threshold to respond to stress, magnitude of response, latency to peak response, and length of time to recovery and return to baseline (Davidson, Jackson, & Kalin, 2000).

Impaired stress reactivity and recovery, like inhibited temperament, may be a shared feature of both RAP and anxiety disorders. To date, there has been only one study that has examined physiological responses to stress in children with RAP and then compared them to children with anxiety. Dorn et al. (2003) compared RAP, anxious and

well children on a number of physiological and psychological indices before, during and after a social and cognitive stress task. They hypothesized that there would be a more robust physiological response to the stressor in RAP and anxious subjects, and that the RAP and anxious children would be indistinguishable from one another. Consistent with their hypothesis, children with RAP and children with anxiety had larger physiological responses, as measured by heart rate and systolic blood pressure, to laboratory stressors than controls. Moreover, both RAP and anxious children had higher stable heart rates than controls, and their systolic blood pressure increased significantly more during the stressor than in the well children. In addition, they found that RAP and anxious children had comparable scores on psychological measures of internalizing symptoms, and their scores were higher than those of controls. In general, children with RAP and children with anxiety looked more similar to each other than to controls on all measures. The relatively small sample size ($n = 14$ per group) and low statistical power may account their failure to find statistically significant differences between the groups on other measures of physiologic response (diastolic blood pressure, levels of salivary cortisol).

Dorn et al. (2003) focused primarily on the sympathetic nervous system's reaction to stress. However, similarities between children with RAP and anxiety may also be found in the parasympathetic nervous system's control over stress recovery. Focusing on parasympathetic functioning in these groups of children may lead to insights into how children with RAP or anxiety recover from stress. One important way to measure this system is by examining the parasympathetic functioning of an individual in both times of rest and stress, specifically by measuring vagal tone.

Heart Rate Variability, Respiratory Sinus Arrhythmia, and Vagal Tone

Changes in the variability of interbeat intervals in heart rate in the respiratory frequency range, called respiratory sinus arrhythmia (RSA), represent a sensitive measure of cardiac stress response and recovery (Porges, 1995). RSA is the best measure of vagal tone, or the influence of the parasympathetic nervous system on heart rate through the vagus nerve. Heart rate is affected by both the sympathetic and parasympathetic nervous system. With each breath, the two systems control heart rate in response to physical and mental states. The SNS is responsible for heart rate acceleration and the PNS for heart rate deceleration. The PNS decelerates heart rate through the afferent and efferent fibers of the vagus nerve. Because vagal efference is inhibitory, activity through these fibers slows the heart rate down. Vagal tone, therefore, is a good measure of the PNS's effect on heart rate. Given that the vagus nerve both regulates stress responses through innervation of the heart and the gastrointestinal tract, it is a good candidate for understanding the mechanisms that may link stress, anxiety and GI symptoms.

Studies have shown that high vagal tone, or high heart rate variability, is a measure of healthy physiological and psychological functioning (e.g., Faulkner, Hathaway, & Tolley, 2003). The autonomic nervous system of individuals with high vagal tone is quick to respond to and recover from stress. During periods of stress, the vagal, or deceleratory, effect on heart rate decreases, and the SNS subsequently increases heart rate. When the stressful situation abates, vagal influence is regained and heart rate decelerates. Low vagal tone, however, indicates little variability in heart rate across time, including periods of stress reactivity and recovery. That is, individuals with low vagal tone tend to show high, stable heart rates across all situations, including during sleep,

during stress, and during times of intense concentration (Beauchaine, 2001).

Several studies have found that adults with anxiety disorders and women with irritable bowel syndrome show significant parasympathetic impairment as measured by vagal tone. For example, Lyonfelds, Borkovec, and Thayer (1995) found that individuals with GAD showed low vagal tone at baseline and low vagal tone (no significant changes) after a mood induction and being exposed to aversive images when compared to non-anxious controls. Similarly, Heitkemper et al. (1998) found that women with IBS had lower vagal tone, had a flattened 24-hr pattern of heart rate variability, and lower levels of vagal tone during sleep. This evidence suggests that the link between RAP and anxiety may lay in parasympathetic dysfunction resulting in a decreased ability to recover from stress. To date, however, no studies have examined vagal tone in children with anxiety disorders or children with RAP.

Coping with Stress in RAP and Anxiety

How children and adolescents attempt to cope with chronic pain and disability may be of critical importance to their general mental health. In samples of children with chronic pain, some studies have shown that maladaptive coping, such as avoidance or disengagement, is strongly associated with depression and disability (e.g., Kashikar-Zuck, Goldschneider, Powers, Vaught, & Hershey, 2001; Kashikar-Zuck, Vaught, Goldschneider, Graham, & Miller, 2002). And, as mentioned previously, pain itself may become a stressor in for children with RAP. Therefore, the way that a child responds to their pain and other stressors may contribute to their overall functioning, well-being, and mental health.

Dual-Process Model of Responses to Stress and Coping

A dual-process model of responses to stress and coping is reflected in a system of involuntary, automatic response processes and a second system of voluntary, controlled responses (Compas et al., 2001). In other words, responses to stress include both automatic and controlled processes. Automatic processes are experienced as uncontrollable, and may or may not be within conscious awareness. Conversely, controlled processes are intentional efforts to regulate and manage sources of stress and are included within the concept of coping. Coping includes only those responses that are controlled, conscious and volitional (Compas et al., 2001). Automatic processes are not considered a coping response; they are included in the broad array of self-regulatory efforts designed to modulate the intensity of an emotion, behavior, thought, or physiological reaction (Compas et al., 2001).

Coping can be further classified as either engagement with or disengagement from the source of stress and one's emotions (e.g., Compas, Connor-Smith, Saltzman, Thomsen, & Wadsworth, 2001; Compas et al., 1997; Skinner, Edge, Altman, & Sherwood, 2003; Skinner & Zimmer-Gembeck, 2007; Tobin, Holroyd, Reynolds, & Wigal, 1989). Engagement responses are oriented toward the source of stress or one's emotions or thoughts. This includes attention to and processing of threat-relevant information; attempts to regulate one's emotional, behavioral, physiological, and cognitive responses to the stressor; and generation and implementation of plans of action to cope with the stress. Engagement responses can be further distinguished along dimensions of control (Compas et al., 2001; Connor-Smith et al., 2000). Primary control

engagement coping involves attempts by the individual to act directly on the pain or other sources of stress or one's emotional responses to a stressor. Examples include problem solving and controlled emotional expression. Secondary control engagement coping responses are strategies directed at adapting to and engaging with pain by regulating attention or cognition. Examples of secondary control engagement coping are cognitive restructuring and acceptance. The third dimension of coping responses is disengagement. Disengagement coping responses are oriented away from the stressor or one's emotions or thoughts. Examples of disengagement include cognitive and behavioral avoidance, denial, and withdrawal.

Walker et al. (1997) describe a similar model of coping defined specifically for children with RAP. In this model, 4 general factors of coping with RAP are defined. The first general factor, Active Coping, includes Problem-Solving, Seeking Emotional Social Support, Seeking Instrumental Support, Using Distraction, Rest, Massage/Guard, and Condition-Specific Strategies (e.g., taking medications prescribed for acid reflux). The second general factor, Passive Coping, includes Behavioral Disengagement, Self-Isolation, and Catastrophizing (e.g., assuming the worst). Finally, the third general factor, Accommodative Coping, includes strategies of Acceptance, Self-Encouragement, Minimizing Pain, and Ignoring Pain. Walker et al. (1997)'s model can be compared to the model detailed above, where primary control engagement coping and "active coping", secondary control engagement coping and "accommodative coping," and disengagement and "passive coping" generally describe similar processes of responding to a stressor. Therefore, for purposes of this paper and despite subtle differences in definition, primary control and active coping, secondary control and accommodative coping, and

disengagement and passive coping will be used to describe the similar types of responses to stress in children with RAP.

Coping with Recurrent Pain Episodes

Studies of children and adolescents coping with acute or chronic pain have generally found that individuals using disengagement coping strategies (e.g., avoidance) and passivity to manage pain or stress experience greater physical and psychological difficulties than their counterparts who use engagement strategies (e.g., Gil, Williams, Thompson, & Kinney, 1991). Conversely, the use of active or engagement coping strategies is associated with better adjustment and adaptation in response to pain episodes. For example, Thomsen et al. (2002) found that amongst children with RAP, those who used primary and secondary control engagement coping responses had fewer somatic complaints and symptoms of anxiety and depression. Additionally, Walker et al. (1997) found that those who self-reported coping by focusing attention on pain (e.g., holding or rubbing the stomach; passive coping) had higher levels of pain and somatization. Similarly, among children with sickle cell disease, parents' reports of children's overall suffering was associated with the children's focusing on pain-related fear and anger as well as catastrophic thinking (Gil, Williams, Thompson, & Kinney, 1991).

Eccleston et al. (2004) investigated the relationship between adolescent distress, parental distress and adolescent coping in a sample of 80 children with chronic or recurrent pain. The children were assessed for pain intensity, anxiety, depression,

disability, and coping using both self- and parent-report. They found that adolescent emotional distress was predicted by their method of coping as measured by the Pain Coping Questionnaire (Reid, Gilbert, & McGrath, 1998). Adolescents who automatically and involuntarily catastrophized and did not attempt to cope with their pain were more likely to endorse symptoms of anxiety and depression and have higher levels of functional disability.

Scharff et al. (2005) used cluster analysis to determine whether subgroups of children with chronic pain (diffuse body pain, limb pain, headache, abdominal pain, back pain, neuropathic pain, “other” pain including chest, testicular, and joint pain) differ on psychological variables and coping. They found that pediatric patients with chronic pain represent a heterogeneous group of individuals, with varying degrees of psychopathology and factors that may contribute to pain and disability. They identified three clusters (“distressed/low functioning, DLF;” “high functioning, HF;” and “family distress, FD”) that corresponded to distress level and functional disability. The FD group endorsed significantly more “Accepting Responsibility” items as a way of coping than the other 2 groups, and adolescents in the DLF group endorsed significantly more Escape/Avoidance coping items than adolescents in the HF group. This study provides more evidence that coping may mediate or moderate the child’s distress and disability in relation to their pain.

Coping and Psychological Symptoms

Coping is also associated with levels of psychological symptoms in children and adolescents (for a review, see Compas et al., 2001). Both internalizing and externalizing

problems are related to increased use of disengagement coping and decreased use of primary and secondary control coping. Though a complete review of research examining the connection between coping and psychological symptoms is beyond the scope of this paper, it is important to acknowledge that the methods that one uses to respond to stressful events in their life may contribute to psychological symptoms, and that these symptoms may also influence the way that one copes with stress.

For example, Thomsen et al. (2002) found that, in a sample of children with RAP, increased use of either primary (active) or secondary (accommodative) control coping was related to decreased levels of anxiety/depression and somatic symptoms. Walker et al. (1997) found that disengagement (passive coping) was significantly positively correlated with somatization, disability and depressive symptoms in children with RAP. In a recent paper examining coping in children with RAP, Compas et al. (2006) used a latent variable analysis of coping using both parent- and child-reports of how children coped with RAP. In a sample of 164 children and adolescents with RAP and their parents, Compas et al. found that children who used secondary control coping strategies, such as acceptance, cognitive restructuring and distraction, showed lower levels of anxiety, depression and somatic complaints. Further, children who used disengagement strategies, such as denial or avoidance, showed increases in psychological and somatic symptoms. Though Compas et al. did not measure physiological variables associated with coping and responses to stress, the evidence that the particular manner in which a child with RAP copes with his or her pain can predict and influence both physiological and psychological symptoms is striking.

Summary. Temperamental characteristics, such as behavioral inhibition, may

influence the processes governing stress reactivity, recovery and coping. Behavioral inhibition has been associated with several key physiological features that influence how an individual responds to and recovers from stress, such as an increased startle response and increase in heart rate. Additionally, parasympathetic functioning as measured by vagal tone has been associated with both anxiety and abdominal pain. Research examining these processes in children is sparse, and to date no study has examined these important psychological and biological features in children with recurrent abdominal pain. An understanding of these psychobiological processes in this population is necessary as it may help to better understand the contributions of anxiety as well as the underlying biological processes that contribute to RAP in children.

Rational for the Current Study and Proposed Hypotheses

The current study examined potential underlying mechanisms that are either common to or discriminate between RAP and anxiety in children. This study is designed to better understand RAP and its relationship with stress and anxiety by using multiple methods to measure stress reactivity, stress recovery, and coping. Specifically, autonomic nervous system processes (heart rate and vagal tone) in response to a social and academic stressor (the Ewart Social Competency Interview; serial subtraction, respectively) and a pain stressor (the cold pressor paradigm) are examined in children with RAP, children with anxiety disorders and healthy controls. Further, symptoms and diagnoses of anxiety are assessed.

The following hypotheses focus on between-group comparisons examining psychological and somatic symptoms, coping, and psychophysiological reactivity to and

recovery from stress. The first three hypotheses investigate overall levels of psychological symptoms and patterns of coping in a population of children with RAP: 1) Children with RAP will have significantly more anxiety symptoms and diagnoses of anxiety disorders than healthy controls as measured by a structured psychiatric interview and questionnaires completed by children and parents. 2) Children with RAP will have significantly higher somatic symptoms than both children with anxiety and healthy control children. 3) Children with RAP and children with anxiety will demonstrate patterns of less adaptive coping compared to healthy controls. That is, children with RAP and children with anxiety are expected to employ significantly more disengagement strategies and fewer primary and secondary control coping strategies.

In order to better understand the relationship between RAP and stress, children with RAP were compared to children with anxiety and a healthy control group on both self-reported and psychophysiological measures of stress reactivity and recovery: 4) Children with RAP and children with anxiety will have higher scores than healthy controls on involuntary engagement responses to stress (e.g., emotional and physiological arousal) based on self-reports of children's responses to social stress. 5) At baseline, children with RAP and children with anxiety will display significantly higher heart rates and lower vagal tone than healthy controls. 6) The RAP and anxiety groups will be significantly more reactive (as measured by heart rate) to the social and cognitive stressor than healthy controls. There will be no differences between the RAP and anxiety groups in stress reactivity. 7) Vagal tone in the RAP and anxiety groups will remain stable throughout exposure to the laboratory stressors (due in part to a floor effect), whereas vagal tone in the healthy control group will decrease during the stressors and return to

baseline at recovery. 8) Children with RAP and children with anxiety will display delayed return to baseline levels of heart rate than healthy controls following the cognitive, social and physical stressors. 9) After exposure to a laboratory analogue of social and academic stress, children with RAP will be significantly higher in pain sensitivity and lower in pain tolerance than children with anxiety or healthy controls in response to the cold pressor task; children with anxiety and healthy controls will not differ from each other on either index of pain responses.

The last three hypotheses focus on within-group analyses of the relations among psychological symptoms, coping, and stress reactivity and recovery among children with RAP, children with anxiety, and healthy controls: 10) Psychological symptoms of anxiety and somatization will be positively correlated with stress reactivity as measured by heart rate, vagal tone, and self-report. 11) Self-reported stress reactivity will be positively correlated with heart rate during the stress tasks and positively correlated with psychological symptoms. 12) Psychological symptoms of anxiety and somatization will be negatively correlated with secondary control coping and positively correlated with disengagement. 13) Stress reactivity, as measured by heart rate, will account for psychological symptoms above and beyond group membership (RAP, Anxious, and Well).

CHAPTER II

METHOD

Participants

Participants included 63 children and adolescents (21 children per group; 29 male, 34 female) ages 8- to 16-years old (mean age 11.64 years) and one parent per child. The mean occupational status, based on the Hollingshead Occupational scores that range from 10 to 90 (Hollingshead, 1975) was 43.22 (SE = 10.46), equivalent to that of administrators, lesser professionals, and proprietors of medium-sized businesses. The sample identified as 71% white, 19% African American, 3% Asian, 6% other, and 2% Hispanic, which is representative of the area of Tennessee from which the sample was drawn. Parent participants included 58 mothers and 5 fathers (mean age 40.56). Of the 87 children and parents approached to participate in the study, 13 were ineligible after the phone screen for the following reasons: the child met criteria for ADHD (n=2), the child was too old to participate (n=1), or the child no longer met criteria for RAP or anxiety (n=10). Eleven eligible families were no longer interested in participating after completing the phone screen.

Children were recruited to represent three groups: children with RAP, children with anxiety, and well children. The groups were matched on gender and age. A phone screen was used to determine eligibility of participants and to determine into which group the child would fall (see below).

Children with RAP were recruited from a tertiary care gastrointestinal clinic at a major Southern academic medical center. Participants were considered eligible for the RAP group if they were diagnosed with functional abdominal pain by a medical doctor and if their pain qualified them to fall into any one of the following ROME-II categories: functional dyspepsia, irritable bowel syndrome, functional abdominal pain, abdominal migraine, or aerophagia (Rasquin-Weber et al., 1999). Further, the abdominal pain must also have occurred at least three times in the past three months and was severe enough to impair functioning or interrupt activities, thus also meeting Apley's (1975) criteria. In our sample, the abdominal pain diagnoses included irritable bowel syndrome, functional dyspepsia, and functional abdominal pain (see Table 1). All of the children in the RAP group (100%) were experiencing abdominal pain with functional disability at least one time per week.

Children with anxiety disorders (anxiety group) were recruited through an outpatient community mental health center and through email advertisements and flyers both in the university medical center and sent to the larger community surrounding the study site. Anxiety group participants were considered eligible if they were currently in or had received past mental health treatment for an anxiety disorder and if they continued to meet criteria for an anxiety disorder.

Finally, healthy control children (well group) were recruited through email advertisements and flyers distributed throughout the community. All well participants were screened for possible anxiety and abdominal pain symptoms over the phone. If the child had received treatment for anxiety or had seen physician for recurrent abdominal pain, they child was considered ineligible for the well group and was re-screened for the

RAP or anxiety groups. None of well group participants originally screened for the study switched groups after screening.

For all three groups, exclusionary criteria included a known chronic health condition, physical handicap, mental retardation, and attention-deficit-hyperactivity disorder (ADHD). ADHD was an exclusionary criterion due to other parts of the study protocol that involved a computer-based attention task.

Measures

Physiological Measures. Heart Rate and vagal tone was measured using BIOPAK physiological data equipment. Fast Fourier Transform (FFT) spectral analyses of the data were conducted and used in data analyses. Physiological data was collected continuously throughout the time the participants were participating in the experimental protocol.

Pain Responses. During the cold pressor task, two pain response measures were taken: pain sensitivity and pain tolerance. Pain sensitivity was recorded at 20 seconds as the number reported from a 10-point Visual Analogue Scale (VAS). Participants who removed their arm before 20 seconds had elapsed rated the pain intensity of the task on the VAS immediately after removing their arm. Pain tolerance was measured as the total time elapsed from the time at which the arm was submerged to the time at which the participant removed their arm.

Anxiety and depression symptoms and somatic problems. The Child Behavior Checklist (CBCL; Achenbach, 1991) was used to assess the participants' levels of symptoms of anxiety and depression and somatic complaints. The CBCL is a 120-item checklist of problem behaviors and competencies that parents rate as not true (0),

somewhat or sometimes true (1), or very true or often true (2) of their child in the past six months. The CBCL assesses internalizing (anxiety/depression, social withdrawal, somatic complaints), and externalizing (aggression, delinquency) emotional and behavioral problems, as well as social and academic competence. In addition, the child self-report version of the CBCL (Youth Self Report, YSR) was administered to children ages 11 and older. Because of their relevance to symptoms associated with RAP (see Garber, Zeman & Walker, 1990; Walker et al., 1993), scores from the anxiety/depression and somatic complaints syndrome scales were used in this study. Data are reported as normalized *T* scores based on separate norms for age and sex, but raw scores were used in the analyses to allow for maximum variance. Reliability and validity of the CBCL and YSR are well established.

In addition, the Multidimensional Anxiety Scale for Children (MASC; March, Parker, Sullivan, Stallings, & Conners, 1997) was also administered to participating parents and children. Children and their parents rate how often each statement is true for the participating child on a 4-point rating scale ranging from “0 = Never true about me” to “3 = Often true about me.” The MASC consists of 39 items distributed across four major factors, three of which can be separated into two additional subfactors each: (1) physical symptoms (tense/restless and somatic/autonomic), (2) social anxiety (humiliation/rejection and public performance fears), (3) harm avoidance (perfectionism and anxious coping), and (4) separation anxiety. In addition, the MASC yields a Total Anxiety Scale, which sums responses to items across the four main scales, and an Anxiety Disorders Index, which sums responses to items that have been found to differentiate children with a diagnosis of an anxiety disorder from children without a

diagnosis. Finally, the Inconsistency Scale screens for inconsistent responding to symptoms. High scores on this scale would indicate that caution is warranted in the interpretation of results from an individual's questionnaire. The MASC has been shown to have excellent internal reliability (e.g., March et al., 1997) and adequate test-retest reliability (e.g., March et al., 1997; March, Sullivan, & Parker, 1999).

Diagnostic Interview. Supplement #1 (Affective Disorders) and Supplement #3 (Anxiety Disorders) of Kiddie-Schedule for Affective Disorders and Schizophrenia for School-Age Children, present and lifetime version (K-SADS-PL) was administered to child participants and their participating parent separately. The K-SADS-PL is a widely used semi-structured, DSM-based psychiatric diagnostic interview with established psychometric properties (Kaufman et al., 1997). It is designed for use in clinical and epidemiologic research to obtain a past and current history of psychiatric disorders in children and adolescents.

Coping and Stress Reactivity. Participants completed the Responses to Stress Questionnaire (RSQ; Connor-Smith, Compas, Wadsworth, Thomsen, & Saltzman, 2000) concerning social stressors. The 57-item RSQ assess coping mechanisms in reference to age-appropriate social stressors and has been shown to have good reliability and validity, including internal consistency with alphas ranging from .73 to .85 (Connor-Smith et al., 2000). The RSQ measures three types of coping: primary control engagement coping (problem solving, emotional expression, emotional regulation), secondary control engagement coping (positive thinking, cognitive restructuring, acceptance, distraction), and disengagement coping (avoidance, denial, wishful thinking); it also measures two types of stress responses: involuntary engagement (rumination, intrusive thoughts,

emotional arousal, physiological arousal, impulsive action) and involuntary disengagement (cognitive interference, involuntary avoidance, inaction, emotional numbing). The Social Stress version of the RSQ (Thomsen et al., 2000) was used in the current study (see Appendix A).

Recurrent abdominal pain symptoms and use of psychological services. Each parent was administered a brief semi-structured interview developed for this study regarding their child's current level and past history of abdominal pain symptoms including diagnoses from their medical provider, functional impairment due to abdominal pain, anxiety, and use of psychological services (See Appendix B). Responses were used to verify the child's current diagnosis of functional RAP, and in order to detail past and current treatment of mental health issues and overall levels of parent-rated anxiety.

Procedure

Parents provided informed consent and child participants provided assent (See Appendix C). All experimental procedures were carried out in two rooms in the Jesup Building on the Peabody Campus of Vanderbilt University. Children participated in the experimental protocol in one room and their parent in another. The rooms were quiet and separated from foot traffic in the building. After informed consent and assent were obtained, children and parents were separated. Parents were administered the K-SADS-PL and completed questionnaires while their child underwent the study protocol.

First, physiological sensors were placed on the child participants' chest in order to record physiological data. Two sensors were placed on the child's sternum to measure heart rate. In addition, a finger sensor collecting galvanic skin response measurements

was placed on the ring finger of the child's left hand. Participants sat quietly for five minutes while baseline physiological data were recorded.

Participants then underwent two psychological stressors. The first is a serial subtraction task designed to mimic an academic stressor. Starting at 400, children are instructed by the experimenter to subtract by 7's for two minutes. Participants are stopped and instructed to start over at 400 when they make a mistake.

After the serial subtraction task is completed, children participated in a social stress interview, based on the one designed by Ewart and Kolodner (1991). The stress interview is a semi-structured interview that allows the subject to re-experience a specific instance that they found stressful. Participants were first shown three cards labeled with topics typically considered stressful to adolescents (school, family, and friends). They were then instructed to order the cards by most stressful to least stressful. Once the cards are ordered, the participants were asked to describe a specific instance that exemplifies the card ranked most stressful. The remainder of the interview consists of the interviewer questioning the participant about the specific details of the incident. The interviewer attempts to lead the participant toward a state of re-experiencing the event through the use of guided imagery, reflective listening, and empathic remarks. This interview has been shown to be a reliable method of eliciting physiological arousal (Ewart & Kolodner, 1991).

The child participants then underwent the Cold Pressor Pain Paradigm (CPP). Before they placed their arm into the cold water, the children were taught how to report how uncomfortable their arm felt by using the Visual Analogue Scale (VAS). The VAS is a vertical scale, in the shape of a ruler, graduated by increments with a sliding

horizontal marker used to represent a continuum from “no pain at all” to “the worst pain imaginable.” The VAS has been established as a valid and reliable measure of pain intensity in children, and has been shown to correlate highly with independent observations of children’s pain behaviors (Zeltzer, Fanurik, & LeBaron, 1989). Unlike parental observer reports, it measures a child’s personal experience of pain intensity to determine how participants differ in subjective pain experience. The participants were asked to report their level of pain using the VAS at 20 seconds. Participants were also informed that if it becomes too uncomfortable to keep their arm in the water they may remove their arm at any time.

Once the children understand the VAS, the cold pressor task commenced. The cold pressor apparatus consisted of an insulated cooler filled with 72 quarts of chilled, circulating water and an arm hammock for placement of the child’s arm into the water. The water circulated 11 pounds of ice (via a submerged Powerhead 802 water pump) at a temperature of 5 degrees Celcius (plus or minus 1 degree). The ice water was circulated for at least five minutes to insure accurate temperature measurement. Data obtained from pilot participants showed that water at a temperature of 5 degrees Celsius produces substantial variance in pain sensitivity and tolerance ratings in children. A four-minute exposure time limit was used during the CPP. After four minutes the CPP ceases to provide any relevant information, as pain responses become confounded with sensations of numbness.

Each child was fitted to the adjustable arm hammock to assure that the proportional surface area of exposed arm is consistent between participants (20 percent of the arm above the elbow). Participants were instructed to (1) immerse their arm in the

cold water, (2) place their arm in the hammock, and (3) remain as still as possible during the experiment. The instruction to cope (i.e., “do or think about whatever is needed to be able keep your arm in the water for as long as you can”) was given. Although they are instructed to “cope”, participants were told they could remove their arms at any time if it becomes too uncomfortable to keep their arms in the water.

As mentioned previously, participants’ levels of tolerance was operationalized as the amount of time elapsed between immersion and removal. To determine how participants differ in subjective pain experience, each subject was asked to report his/her level of pain using the VAS at 20 seconds. Participants also reported their pain levels (using the VAS) at the time they remove their arms from the CPP to provide a measure of the subjective levels of pain that prompted removal of the arm from the cold water.

Participants were then given the opportunity to complete questionnaires in the lab in exchange for a \$40 gift certificate to Target. When the child finished, the parent rejoined the child the family was given \$75 cash compensation and (if the child completed the questionnaires) a \$40 gift certificate to Target. Participants were then debriefed and given a visual explanation of their physiological data.

Statistical Power

For the proposed study, power calculations were based on effect sizes from the only study that has compared children with RAP, children with anxiety, and well children (Dorn et al., 2003). Power estimates for the proposed study were therefore based on estimates of medium effects with a power of .85 and an alpha coefficient of .05. Based on these anticipated effect sizes, 25 participants will be required for each group (children

with RAP, children with anxiety, and healthy controls) to detect differences of this magnitude or larger. Due to difficulties in recruitment of anxious participants, each group will contain 21 participants matched by age and gender.

CHAPTER III

RESULTS

Comparison on Overall Levels of Anxiety and Somatic Symptoms

In order to assess group differences in overall levels of anxiety symptoms and diagnoses, an Analysis of Variance (ANOVA) with a Bonferonni correction to correct for family-wise error rate was applied to each set of inter-related analyses (adjusted $p < .02$) in order to determine whether the three groups (RAP, anxious, and well) differed on the various subscales of the CBCL, YSR, and parent and child versions of the MASC. If significant, independent t -tests were used to conduct paired comparisons between two groups at a time on each variable. Cohen's d effect size calculations (Cohen, 1988) were performed for all significant between-group differences. Effect sizes less than 0.2 indicate a negligible effect, those between 0.2 and 0.5 indicate a small effect, those between 0.5 and 0.8 indicate a medium effect, and those greater than 0.8 are considered large effects. For diagnostic data provided by the K-SADS-PL, Chi-square analyses were used to compare groups on total number of participants currently qualifying for an anxiety disorder diagnosis.

Recurrent abdominal pain symptoms and use of psychological services. Table 1 lists the frequencies of parent-reported abdominal pain and subsequent functional impairment in their child including use of medications and diagnosis (if known). All children with RAP reported having had 3 or more stomachaches in the last three months with associated functional impairment (interference with school, activities, and/or eating).

Therefore, each child in the RAP group met Apley's (1975) criteria for RAP as well as Rome II criteria for functional abdominal pain unless otherwise specified (e.g., the child met criteria for Irritable Bowel Syndrome). Twenty-nine percent of children with anxiety (n = 6) reported having 3 or more stomachaches in the past 3 months with subsequent functional impairment. No well children reported stomachaches in the previous 3 months.

Table 1. Recurrent abdominal pain symptoms and associated functional disability

	In the last 3 months, how often has your child had a stomachache?	Did stomachaches interfere with school (such as missing days of school)?	Did stomachaches interfere with activities (such as hobbies, spending times with friends, etc.)?	Did stomachaches interfere with eating (such as eating less, changing the child's diet, etc.)?	Does the child take medications for their stomachaches?	Has the child ever received a diagnosis for their gastrointestinal symptoms?
RAP Group	Never = 0 (0%) 1-2x's = 0 (0%) 3+x's = 21 (100%)	No = 7 (33.3%) Yes = 14 (67%)	No = 7 (33.3%) Yes = 14 (67%)	No = 4 (19%) Yes = 17 (81%)	No = 4 (19%) Yes/OTC = 12 (57%) Yes/Prescribed = 1 (4.8%) Yes/Both OTC & Prescribed = 4 (19%)	No = 8 (38%) Yes/Irritable Bowel Syndrome = 5 (24%) Yes/Other Functional = 8 (38%)
Anxious Group	Never = 12 (57.1%) 1-2x's = 3 (14.3%) 3+x's = 6 (28.6%)	No = 17 (81%) Yes = 4 (19%)	No = 17 (81%) Yes = 4 (19%)	No = 18 (85.7%) Yes = 3 (14.3%)	No = 15 (71.4%) Yes/OTC = 6 (28.6%) Yes/Prescribed = 0 (0%) Yes/Both OTC & Prescribed = 0 (0%)	No = 18 (85.7%) Yes/Functional Dyspepsia = 1 (4.8%) Yes/Other Functional = 2 (9.5%)
Well Group	Never = 21 (100%) 1-2x's = 0 (0%) 3+x's = 0 (0%)	No = 21 (100%) Yes = 0 (0%)	No = 21 (100%) Yes = 0 (0%)	No = 21 (100%) Yes = 0 (0%)	No = 21 (100%)	No = 0 (100%)

Note: Results reported by number of children followed by percentages per group. Note: OTC = Over the counter.

Parents were asked whether their child ever had or currently has any difficulty with anxiety, worrying or fears. Eighty-one percent of parents of children with RAP answered “yes” to this question ($n = 17$), compared to 100% of parents of children with anxiety and 0% of parents of well children. Thirty-eight percent of children with RAP ($n = 8$) had received in the past or currently received psychological services for anxiety.

YSR/CBCL subscale comparisons. Means and standard deviations of YSR ($n = 37$) and CBCL ($n = 63$) data are presented in Table 2. On the anxiety/depression subscale of the YSR, there was a trend for children with RAP to report significantly more symptoms than well children, $t(20) = 1.95, p = .07$. Children with RAP reported significantly more somatic complaints on the YSR than both well children, $t(20) = 3.41, p < .005, d = 1.4$, and anxious children, $t(20) = 3.32, p < .005, d = 1.0$. Children with RAP endorsed significantly more total internalizing symptoms than well children, $t(20) = 2.76, p < .05, d = 1.29$, and significantly less than anxious children, $t(20) = 2.03, p = .05, d = .72$.

Similar results were found on the CBCL; parents of children with RAP rated their child as having significantly more symptoms of anxiety and depression, $t(40) = 2.14, p < .05, d = .57$, somatic complaints, $t(40) = 4.69, p < .001, d = 1.56$, and total internalizing symptoms than well children, $t(40) = 4.03, p < .001, d = 1.37$. Children with RAP and anxious children did not differ on the CBCL somatic complaints and total internalizing symptoms scales. Children with anxiety disorders displayed significantly higher scores on the anxiety/depression subscale of the CBCL when compared to children with RAP, $t(40) = 2.95, p < .005, d = 1.01$, but not on the total internalizing subscale.

The three groups were also compared on DSM-IV-based subscales of the CBCL and YSR. On the YSR, children with RAP reported significantly more symptoms on DSM Somatic Problems than both well and anxious children $t(20) = 2.99, p < .005, d = 1.28$; $t(20) = 2.73, p < .01, d = .89$. Children with RAP did not endorse more symptoms than well children on the DSM Affective and Anxiety Problems subscales.

Children with RAP were rated by their parents significantly higher than well children on CBCL DSM Affective Problems, $t(40) = 1.99, p < .05, d = .60$, Anxiety Problems, $t(40) = 2.31, p < .05, d = .66$, and Somatic Problems, $t(40) = 4.5, p < .001, d = 1.55$. Children with anxiety were rated significantly higher than children with RAP, $t(40) = 2.24, p < .05, d = .78$, and well children, $t(2,60) = 3.56, p < .001, d = 1.30$, on the CBCL DSM Anxiety Problems subscale. However, children with anxiety and children with RAP did not differ on DSM Affective and Somatic Problems subscales of the CBCL, though anxious children were rated significantly higher than well children on these two subscales, $t(40) = 2.67, p < .01, d = .86$; $t(40) = 3.56, p < .001, d = .94$, respectively.

Table 2. CBCL and YSR Means, Standard Deviations and Effect Sizes Between Groups

	RAP		Anxious	Well	F-Scores	Cohen's <i>d</i> :		Cohen's <i>d</i> : Anx vs. Well
	(n=12)	(n=15)	(n=15)	(n=10)		RAP vs Anx	RAP vs. Well	
<i>YSR</i>								
Anxious/Depressed	56.8(6.0) ^a	56.8(6.4) ^a	52.4(2.3) ^b	F(2, 34) = 2.2, p = .13	0	1.06	1.01	
Somatic Complaints	61.8(5.6) ^a	56.0(6.0) ^b	54.6(4.9) ^b	F(2, 34) = 7.3, p < .002	1.0	1.37	.26	
Total Internalizing	59.6(5.4) ^a	54.9(7.6) ^b	49.9(9.6) ^c	F(2, 34) = 4.2, p < .05*	.72	1.94	.58	
DSM Affective Problems	57.0(5.7) ^a	54.5(5.4) ^a	54.1(5.3) ^a	n.s.	.45	.53	.07	
DSM Anxiety Problems	55.3(6.4) ^a	58.0(7.0) ^a	52.9(4.1) ^a	n.s.	.40	.46	.92	
DSM Somatic Problems	61.9(5.4) ^a	56.7(6.3) ^b	55.7(4.3) ^b	F(2, 34) = 5.21, p < .01	.89	1.28	.19	
<i>CBCL</i>								
Anxious/Depressed	56.5(5.3) ^a	63.8(9.5) ^b	53.6(4.9) ^c	F(2, 60) = 12.1, p < .001	.98	.57	1.42	
Somatic Complaints	63.3(8.5) ^a	60.1(10.2) ^a	53.4(4.2) ^b	F(2, 60) = 7.5, p < .001	.34	1.56	.93	
Total Internalizing	59.6(6.3) ^a	61.1(10.5) ^a	48.2(10.3) ^b	F(2, 60) = 4.4, p < .05*	.18	1.37	1.24	
DSM Affective Problems	57.0(6.1) ^a	59.7(9.1) ^a	53.6(5.1) ^b	F(2, 60) = 4.5, p < .05*	.36	.61	.86	
DSM Anxiety Problems	56.6(5.5) ^a	62.4(9.4) ^b	53.2(4.8) ^c	F(2, 60) = 8.4, p < .001	.78	.66	1.30	
DSM Somatic Problems	63.5(9.0) ^a	60.4(10.9) ^a	53.3(4.2) ^b	F(2, 60) = 7.1, p < .002	.31	1.55	.94	

Note: Data are presented as normalized *T*-scores. Those columns with differing superscripts are significantly different.

* After Bonferroni correction, this difference is no longer considered significant.

MASC subscale comparisons. Means and standard deviations of parent- and child-reports on the MASC are presented in Table 3. On the MASC, parents of children with RAP rated their children as significantly higher than well children on the following scales: Somatic/Autonomic, $t(40) = 3.18, p < .01, d = 1.0$, Perfectionism, $t(40) = 2.03, p < .05, d = .64$, Separation/Panic Scale, $t(40) = 3.49, p < .001, d = 1.15$, and Anxiety Disorder Index, $t(40) = 2.65, p < .01, d = .83$. Children with RAP rated themselves as significantly higher than well children only on the Separation/Panic subscale, $t(40) = 3.50, p < .001, d = 1.13$. When compared to children with anxiety disorders, children with RAP did not rate themselves differently on any of the self-reported indices. However, parents of anxious children rated their child significantly higher than parents of children with RAP on the Physical Symptoms Scale, $t(40) = 2.23, p < .05$, Tense/Restless, $t(40) = 2.99, p < .01, d = .96$, Social Anxiety Scale, $t(40) = 2.07, p < .05, d = .74$, and Anxiety Disorder Index subscales, $t(40) = 2.10, p < .05, d = .75$. Parents of anxious children rated their child significantly higher than parents of well children on the Somatic/Autonomic, $t(40) = 2.30, p < .05, d = .99$, Physical Symptoms, $t(40) = 2.23, p < .05, d = .84$, Humiliation/Rejection, $t(40) = 2.98, p < .01, d = 1.0$, Performing in Public, $t(40) = 3.13, p < .01, d = .79$, Social Anxiety, $t(40) = 3.57, p < .001, d = 1.1$, Separation/Panic subscales, $t(40) = 4.85, p < .001, d = 1.64$, and Anxiety Disorder Index, $t(40) = 4.85, p < .001, d = 1.5$.

Table 3. MASC Means, Standard Deviations, and Effect Sizes Between Groups

	Cohen's <i>d</i> :			<i>F</i> -Scores	Cohen's <i>d</i> :		
	RAP	Anxious	Well		RAP vs Anx	RAP vs. Well	Anx vs. Well
<i>Child-Report</i>							
Physical Symptoms Scale	49.1(7.2)	48.1(7.5)	47.5(8.8)	n.s.	.14	.20	.07
<i>Tense/Restless</i>	49.6(9.2)	49.2(8.8)	49.3(8.3)	n.s.	.04	.03	.01
<i>Somatic Autonomic</i>	48.5(6.2)	47.2(7.2)	45.8(8.6)	n.s.	.19	.36	.18
Harm Avoidance Scale	50.1(9.8)	51.7(9.6)	51.5(10.5)	n.s.	-.16	-.14	.02
<i>Perfectionism</i>	49.4(7.8)	49.7(7.6)	48.7(10.9)	n.s.	-.04	.07	.11
<i>Anxious Coping</i>	50.7(10.8)	52.8(10.6)	53.4(9.5)	n.s.	-.20	-.27	.06
Social Anxiety Scale	54.6(12.1)	50.2(8.4)	54.5(12.1)	n.s.	.43	.01	-.42
<i>Humiliation/Rejection</i>	54.4(14.1)	49.3(8.8)	53.6(12.5)	n.s.	.45	.06	-.40
<i>Performing in Public</i>	53.6(10.7)	51.5(8.4)	54.6(10.6)	n.s.	.22	-.09	.32
Separation/Panic Scale	56.6(8.6) ^a	53.8(9.2) ^a	47.3(7.8) ^b	F(2,60) = 5.5, p < .01	.31	1.13	.76
Anxiety Disorder Index	53.0(9.8)	50.0(8.1)	49.9(9.6)	n.s.	.34	.32	.01
<i>Parent-Report</i>							
Physical Symptoms Scale	42.4(5.2) ^a	45.0(6.5) ^b	40.4(4.4) ^a	F(2,60) = 2.7, p < .10	-.44	.42	.84
<i>Tense/Restless</i>	39.5(4.7) ^a	44.8(6.3) ^b	41.7(5.8) ^a	F(2,60) = 4.3, p < .05*	-.96	-.42	.51
<i>Somatic Autonomic</i>	46.8(7.3) ^a	46.0(7.7) ^a	41.0(4.4) ^b	F(2,60) = 4.6, p < .05*	.11	.99	.83
Harm Avoidance Scale	49.4(7.1)	51.2(8.3)	45.8(10.1)	n.s.	-.23	.42	.59
<i>Perfectionism</i>	53.4(7.7) ^a	53.9(9.7) ^a	48.0(9.4) ^b	n.s.	-.05	.60	.59
<i>Anxious Coping</i>	46.6(8.1)	48.8(10.6)	45.4(9.7)	n.s.	-.24	.13	.33
Social Anxiety Scale	52.5(8.7) ^a	59.9(11.3) ^b	47.8(11.5) ^a	F(2,60) = 5.8, p < .01	-.74	.49	1.06
<i>Humiliation/Rejection</i>	54.7(9.2) ^a	61.7(11.6) ^b	49.4(12.8) ^a	F(2,60) = 5.3, p < .01	-.67	.48	1.01
<i>Performing in Public</i>	49.3(9.4) ^a	55.0(13.4) ^b	46.2(9.0) ^a	F(2,60) = 3.2, p < .05*	-.50	.34	.79
Separation/Panic Scale	55.9(10.7) ^a	59.5(13.5) ^a	44.8(8.7) ^b	F(2,60) = 7.7, p < .001	-.30	1.14	1.32
Anxiety Disorder Index	46.8(8.4) ^a	53.0(8.1) ^b	40.1(7.6) ^c	F(2,60) = 11.5, p < .001	-.75	.84	1.64

Note: Data are presented as normalized *T*-scores. Those columns with differing superscripts are significantly different.

* After Bonferroni correction, this difference is no longer considered significant.

Anxiety Disorders

Sixty-seven percent of children with RAP met criteria for an anxiety disorder, compared to 100% of children with anxiety disorders, $\chi^2(1) = 8.40, p < .01$, and 6% of well children, $\chi^2(1) = 14.54, p < .001$. The most prevalent disorders in children with RAP were Generalized Anxiety Disorder (GAD, $n = 10, 48\%$), Specific Phobia ($n = 7, 33\%$), Social Phobia ($n = 5, 24\%$) and Separation Anxiety Disorder (SAD, $n = 5, 24\%$) (see Figure 1). Because GAD and SAD both include stomachaches as part of their criteria, the data were re-analyzed excluding those symptoms from the total number of symptoms qualifying the participant for the diagnosis. The percentage of children with RAP meeting criteria for these two disorders remained the same (48% and 24%, respectively).

Coping and Self-Reported Responses to Stress

Means and standard deviations of the ratio scores on the RSQ are presented in Table 4. There was a trend for children in the RAP group to report lower use of secondary control coping and disengagement than the Well and Anxious groups, $F(2,57) = 3.01, p = .058$; $F(2,57) = 2.45, p = .096$, partially confirming the hypothesis that children with RAP would display less adaptive coping than healthy controls. T-tests showed that children with RAP reported significantly lower levels of secondary control coping than the anxious children ($t(35) = -2.99, p < .005$) and significantly lower levels of disengagement than the well children ($t(36) = 1.98, p < .05$). Importantly, children in the RAP group reported significantly higher amounts of Involuntary Engagement than the well and anxious groups ($F(2,57) = 5.01, p < .01$). T-tests confirmed this finding (RAP vs. Well, $t(36) = -2.31, p < .05$; RAP vs. Anxious, $t(35) = 3.54, p < .001$), thus

supporting the hypothesis that children with RAP would report that they experience increased emotional and physiological arousal in response to stress.

Table 4. RSQ Means, Standard Deviations and Between Group Comparisons

	RAP	Anxious	Well	<i>F</i> -Scores
Primary Control	.19(.03)	.18(.03)	.18(.05)	n.s.
Secondary Control	.23(.04) ^a	.27(.04) ^b	.25(.05) ^a	$F(2,57) = 3.01, p = .058$
Disengagement	.14(.02) ^b	.15(.02) ^a	.16(.03) ^a	$F(2,57) = 2.45, p = .096$
Inv. Engagement	.26(.04) ^b	.22(.03) ^a	.23(.04) ^a	$F(2,57) = 5.01, p < .01$
Inv. Disengagement	.17(.03)	.17(.03)	.17(.03)	n.s.

Note: Those columns with differing superscripts are significantly different.

Physiological Variables at Baseline and in Response to Laboratory Stress Tasks

A series of one-way ANOVA's were conducted in order to determine whether the three groups differed at any of the 5 time points in the study (baseline, serial subtraction, social stress interview, cold pressor, and recovery) on the various physiological measures (heart rate, low frequency, and high frequency). The means and standard deviations of these variables are presented in Table 5. T-tests were then used to compare groups on each variable at each time period.

Table 5. Physiological Variables by Time Point Means, Standard Deviations, and Between Group Comparisons

Time Period	n	RAP Mean (SD)	n	ANX Mean (SD)	n	Well Mean (SD)	F-Scores
<i>Heart Rate</i>							
Baseline	17	88.07(7.82) ^a	19	87.84(11.55) ^a	15	82.15(5.36) ^b	$F(2,48) = 2.27, p = .12$
Serial Subtraction	18	92.47(10.84)	19	87.13(9.08)	16	86.98(7.36)	$F(2,54) = 1.92, p = .16$
Social Stress Interview	17	91.26(7.71)	19	88.33(11.00)	16	87.84(6.97)	$F(2,49) = .73, p = .49$
Cold Pressor	15	93.63(5.98) ^b	11	85.77(7.98) ^a	12	84.29(9.16) ^a	$F(2,35) = 5.87, p = .006$
Recovery	17	87.61(8.06)	17	86.06(8.24)	16	83.94(6.62)	$F(2,47) = .83, p = .44$
<i>Low Frequency</i>							
Baseline	18	939.44(663.01) ^a	19	1,042.36(746.58) ^a	17	1,497.00(1056.93) ^b	$F(2,51) = 2.21, p = .12$
Serial Subtraction	18	2,058.65(1420.50)	17	1,849.27(1242.30)	16	2,235.64(1428.18)	$F(2,48) = .38, p = .69$
Social Stress Interview	18	1,394.02(700.90)	18	1,526.11(1054.11)	15	1,356.06(718.74)	$F(2,48) = .19, p = .83$
Cold Pressor	15	1,331.76(871.51)	10	1,002.08(340.48)	12	1,249.78(676.06)	$F(2,34) = .68, p = .51$
Recovery	18	1,772.84(1,075.09)	15	1,592.4(844.30)	17	2,046.83(1428.18)	$F(2,47) = .64, p = .53$
<i>High Frequency</i>							
Baseline	18	1,018.50(1208.21)	18	779.71(772.39)	17	1,217.54(830.40)	$F(2,50) = .92, p = .41$
Serial Subtraction	18	1,397.26(919.06) ^a	17	1,169.55(735.25) ^b	17	1,853.01(1104.50) ^a	$F(2,52) = 2.38, p = .10$
Social Stress Interview	18	710.09(457.86)	18	787.02(690.86)	16	828.11(512.89)	$F(2,49) = .19, p = .83$
Cold Pressor	16	981.13(1104.84)	11	683.09(442.43)	11	1,255.18(1039.75)	$F(2,35) = 1.01, p = .37$
Recovery	16	1,067.68(920.61)	17	1,057.93(997.27)	16	1,474.00(1,188.62)	$F(2,46) = .84, p = .43$

Note: Those columns with differing superscripts are significantly different.

Heart Rate. A group x time repeated measures ANOVA was used to compare groups on heart rate at each of the 5 time points of the study (i.e., baseline, serial subtraction, social stress interview, cold pressor, and recovery). There was a significant main effect for time ($F(3,22) = 4.60, p < .01$), but no group by time interaction. However, based on a priori hypotheses, group comparisons were made at each of the five time points in order to determine difference between groups that may have been masked in the group x time ANOVA. In fact, at three of the five time points, there was either a significant between-group difference or a trend for a difference on mean beats per minute (heart rate; see Table 5). The RAP group displayed a significantly higher heart rate than the well group at baseline ($t(30)=-2.46, p < .02$). Compared to the well group, there was a trend for the Anxious group to also display a significantly higher heart rate at baseline ($t(32)=-1.76, p = .088$). The RAP and anxious groups did not differ in baseline heart rate. The RAP group continued to show a higher heart rate than the well group during serial subtraction ($t(32)=-1.70, p = .098$) and during the cold pressor ($t(25)=-3.20, p < .005$). The well group did not differ from the anxious group during any other time period. The RAP group showed a significantly higher heart rate than the anxious group during the cold pressor ($t(24)=2.88, p < .010$).

Vagal tone measures of high frequency (HF) and low frequency (LF) showed no significant differences between groups at any of the time points during the laboratory study except for a trend for the RAP group to be lower in LF than the well group at baseline ($t(33)=1.88, p = .069$) and for the anxious group to be significantly lower in HF than the Well group during Serial Subtraction ($t(32)=2.12, p < .04$). This may be due in part to difficulty cleaning, exporting and analyzing the vagal tone data. Further, other

research studies that examine vagal tone in both children and adults use a significantly longer baseline time interval and longer study period epochs that allow for a proper Fast Fourier Transform (FFT) to be conducted on the EKG data (e.g., Olafsdottir, Ellertsen, Berstand, & Fluge, 2001). The difficulties in analyzing and interpreting this data are explored in the Discussion section below.

Pain Sensitivity and Pain Tolerance

Means and standard deviations of Pain Scale Rating (pain sensitivity) and total time the child's arm was immersed in the cold pressor (pain tolerance) are listed in Table 6. Children with RAP had a significantly higher mean rating of pain sensitivity compared to the anxious group ($F(2, 54) = 3.70; p < .05, d = 1.0$). The healthy control group was not significantly different from either the RAP or anxious groups. The three groups did not differ on pain tolerance, indicating that despite having their arms in the cold pressor for, on average, the same amount of time, children with RAP reported the cold pressor to be significantly more painful than the well and anxious children.

Table 6. Cold Pressor Pain Ratings

	RAP	Anxious	Well	<i>F</i> -Score
Pain Intensity	6.75(2.24) ^a	4.55(2.23) ^b	5.43(2.93)	$\underline{F}(2,54) = 3.70, p < .05$
Pain Tolerance (sec)	77.62(84.24)	65.60(64.60)	79.95(94.34)	n.s.

Note: Those columns with differing superscripts are significantly different.

Associations Between Psychological and Physiological Symptoms

Pearson product-moment coefficient correlations were used to understand the possible relations between physiological reactivity to stress, psychological symptoms, and self-reported stress reactivity. Tables 7, 8, and 9 show the correlations among heart rate, measures of internalizing and somatic symptoms, and the subscales of coping and involuntary stress responses on the RSQ.

Correlations Between Psychological Symptoms, Coping and Reactivity to Stress.

Hypothesis 10, which predicted that heart rate would be positively correlated with psychological and somatic symptoms, was confirmed. Baseline heart rate was significantly and positively correlated with the CBCL Anxious/Depressed, Somatic Complaints, and Total Internalizing subscales (see Table 7), as well as the YSR Anxious/Depressed subscale (see Table 8) and the parent-reported MASC humiliation/rejection subscale. Heart rate during serial subtraction was significantly positively correlated with the CBCL Somatic Complaints and Total Internalizing subscales, the YSR Anxious/Depressed subscale and the child-reported MASC Harm Avoidance subscale. Heart rate during the social stress interview was significantly positively correlated with the CBCL Somatic Complaints subscale, the YSR Anxious/Depressed subscale, and the child-reported MASC Anxious Coping and Harm Avoidance subscales. Finally, heart rate during the cold pressor was significantly positively correlated with the parent-reported MASC Social Anxiety subscale and the child-reported MASC Separation/Panic subscale.

Hypothesis 11, which predicted that coping would be negatively related to physiological stress reactivity, was partially confirmed. That is, secondary control coping is significantly negatively correlated with heart rate during serial subtraction, the social stress interview, and during the cold pressor. Finally, as predicted, self-reported stress reactivity (involuntary engagement; physiological arousal, emotional arousal, intrusive thoughts) is significantly positively correlated with heart rate at all 4 time intervals (see Table 9).

Table 7. Correlations Between Heart Rate and CBCL Subscales

	1.	2.	3.	4.	5.	6.	7.
1. CBCL Anx/Dep	--						
2. CBCL Som. Comp.	.523**	--					
3. CBCL DSM Anx.	.867**	.547**	--				
4. CBCL DSM Som.	.537**	.966**	.550**	--			
5. HR Baseline	.336*	.443**	.363**	.375**	--		
6. HR Serial Sub.	.219	.366**	.228	.290*	.692**	--	
7. HR Social Str. Int.	.230	.300*	.176	.212	.763**	.847**	--
8. HR Cold Pressor	-.018	.310	.047	.259	.480**	.371*	.604**

* $p < .05$ ** $p < .01$

Table 8. Correlations Between Heart Rate and YSR Variables

	1.	2.	3.	4.	5.	6.	7.
1. YSR Anx/Dep	--						
2. YSR Som. Comp.	.263	--					
3. YSR DSM Anx.	.838**	.138	--				
4. YSR DSM Som.	.185	.896**	.078	--			
5. HR Baseline	.507**	.139	.380*	.157	--		
6. HR Serial Subt.	.511**	.147	.352	.221	.692**	--	
7. HR Social Str. Int.	.484**	.148	.315	.136	.763**	.847**	--
8. HR Cold Pressor	.247	.237	.098	.219	.480**	.371*	.604**

* $p < .05$ ** $p < .01$

Table 9. Correlations Between Heart Rate and RSQ Subscales

	1.	2.	3.	4.	5.	6.	7.	8.
1. Primary Control	--							
2. Secondary Control	.361**	--						
3. Disengagement	-.510**	-.300*	--					
4. Inv. Engagement	-.465**	-.731**	-.103	--				
5. Inv. Diseng.	-.670**	-.683**	.334*	.384**	--			
6. HR Baseline	-.040	-.156	-.124	.348*	-.031	--		
7. HR Serial Subt.	.100	-.295*	-.257	.495**	-.055	.692**	--	
8. HR Social Str. Int.	.088	-.296*	-.170	.426**	-.027	.763**	.847**	--
9. HR Cold Pressor	.152	-.310	-.101	.375*	-.088	.480**	.371*	.604**

* $p < .05$ ** $p < .01$

Correlations Between Coping and Psychological and Somatic Symptoms. As

predicted, secondary control coping was significantly negatively correlated with the YSR Anxious/Depressed, Somatic Complaints, and Total Internalizing subscales (see Table 10). Secondary control coping was also significantly negatively correlated with the child-reported MASC Tense/Restless and Physical Symptoms subscales. Further, the Involuntary Engagement scale of the RSQ significantly positively correlated with the YSR Anxious/Depressed, Somatic Complaints, and Total Internalizing subscales as well as the child-reported MASC Tense/Restless, Physical Symptoms, and Separation/Panic subscales.

Table 10. Correlations Between RSQ Subscales and CBCL/YSR Subscales

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.
1. Primary Control	--										
2. Secondary Control	.361**	--									
3. Disengagement	-.510**	-.300*	--								
4. Involuntary Eng.	-.465**	-.731**	-.103	--							
5. Involuntary Dis.	-.670**	-.683**	.334*	.384**	--						
6. CBCL Anx/Dep	-.004	.214	.000	-.080	-.201	--					
7. CBCL Som. Comp.	.000	-.009	-.117	.143	-.085	.523**	--				
8. CBCL DSM Anx.	.005	.209	.017	-.038	-.271*	.867**	.547**	--			
9. CBCL DSM Som.	-.017	-.006	-.077	.106	-.055	.537**	.966**	.550**	--		
10. YSR Anx/Dep	-.188	-.393*	.082	.419**	.176	.322	.323	.308	.290	--	
11. YSR Som. Comp.	-.021	-.417*	-.154	.354*	.279	-.004	.150	-.069	.130	.263	--
12. YSR DSM Anx.	-.067	-.103	.023	.134	.030	.379*	.193	.423**	.186	.838**	.138

* $p < .05$ ** $p < .01$

Correlations Between Pain Intensity and Somatic Symptoms. Pain Intensity

correlated positively and significantly with YSR Somatic Complaints ($r = .44, p < .01$) and YSR DSM Somatization ($r = .36, p < .05$), but not with CBCL Somatic Complaints or DSM Somatization.

Contributions of Group and Physiological Stress Reactivity on Psychological Symptoms

An Analysis of Covariance (ANCOVA) was conducted in order to assess whether physiological stress reactivity would account for psychological symptoms above and beyond group membership (RAP, anxious, and well)¹. Groups were compared on psychological symptoms (YSR and CBCL anxious/depressed, somatic complaints, DSM Anxiety, and DSM Somatization subscales) covarying for mean heart rate of the two stress tasks combined (serial subtraction and the social stress interview). For all four CBCL variables, there was a significant difference between groups after controlling for heart rate during the stress tasks (CBCL Anxious/Depressed, $F(2, 47) = 10.52, p < .001$; CBCL Somatic Complaints, $F(2, 47) = 5.53, p = .007$; CBCL DSM Anxiety, $F(2,47) = 7.84, p = .001$; CBCL DSM Somatization, $F(2, 47) = 4.84, p = .01$). Further, mean heart rate as a covariate significantly and independently accounted for differences in the variance of CBCL Anxious/Depressed scores ($F(1, 51) = 5.66, p = .02$) and there was a trend for differences on the CBCL Somatic Complaints ($F(1, 51) = 3.69, p = .06$) and CBCL DSM Anxiety subscales ($F(1, 51) = 3.55, p = .07$). Therefore, although heart rate reactivity is related to several CBCL subscales, the differences between groups remain significant after accounting for heart rate differences. On the YSR subscale group

¹ Multiple regression analyses were also conducted predicting the same dependent variables. Overall, the findings are consistent with the results of the ANCOVA's.

comparisons, there continued to be a significant difference between groups on the YSR Somatic Complaints ($F(1,26) = 5.69, p = .01$) and DSM Somatization ($F(1,26) = 3.72, p = .04$) after controlling for mean heart rate during the stress tasks as a covariate. As in the ANOVA, the anxious/depressed and DSM anxiety scales remained insignificant. However, mean heart rate during the stress tasks did significantly and independently account for differences in the variance of those two YSR subscales (anxious/depressed, $F(1,26) = 7.74, p = .01$; DSM anxiety, $F(1, 26) = 4.84, p = .04$), but not on the YSR somatic complaints or DSM somatization scales. It should be noted that the power for the analyses on the YSR were greatly reduced by the small sample size of those children eligible to fill out the YSR as well as missing heart rate data during the stress tasks.

CHAPTER IV

DISCUSSION

Recurrent abdominal pain (RAP) is a highly prevalent childhood pain condition that is associated with increased health care use and functional disability (Campo & Fritsch, 1994; Hyams, Burke, Davis, Rzepski, & Andrulonis, 1996). Clinicians and researchers have postulated an association between anxiety and RAP in children (e.g., Apley, 1975; Scharff, 1997). This study examined some of the psychological and psychophysiological factors and processes that may influence RAP in children. A central hypothesis of this study is that anxiety and reactivity to stressful events are critical psychological factors in pediatric RAP.

Association Between RAP and Anxiety Symptoms and Disorders

Using self- and parent-report questionnaires and diagnostic interviews, children with RAP were compared to a group of children with anxiety disorders and a healthy control group. It was hypothesized that children with RAP would display significantly more anxiety and somatic symptoms and meet criteria for anxiety disorders more often than healthy controls. Consistent with these hypotheses, questionnaire data showed that parents of children with RAP rated their child as significantly higher than well children on measures of anxiety, affective problems, and somatic symptoms. Also on parent measures, children with RAP were nearly indistinguishable from children with anxiety on measures of anxiety and somatic symptoms. Self-report data showed similar results

where children with RAP rated themselves as significantly higher on somatic complaints and marginally higher on symptoms of anxiety and other internalizing symptoms as compared to well children, although these differences were not as pronounced as those found in parents' reports of their children's symptoms. Similar to the analyses of parents' reports, RAP and anxious children did not differ on self-report questionnaire data.

In addition to questionnaire data, this study used semi-structured diagnostic interviews in order to uncover whether children in the sample met criteria for an anxiety disorder. Diagnostic data from this study revealed that children with RAP were significantly more likely to have an anxiety disorder diagnosis than healthy controls. Sixty-seven percent of children with RAP met criteria for an anxiety disorder, with 48% meeting criteria for GAD. Specific Phobia, Social Phobia, and Separation Anxiety Disorder were also prevalent. When somatic symptoms associated with GAD and Separation Anxiety Disorder were controlled for, children with RAP continued to meet criteria for these diagnoses. The National Comorbidity Replication Study places the lifetime prevalence of any anxiety disorder in the general adult population at 18.1% (Kessler, Chiu, Demler, & Walters, 2005). In children, the true prevalence rates of anxiety disorders are less well established, but have been reported to be at approximately 8-10% (e.g., Costello et al., 2003; Fergusson, Horwood, & Lynskey, 1993; Lewisohn et al., 1993). Therefore, in addition to being higher than the rates in the sample of healthy control participants, the lifetime prevalence of anxiety disorders in this sample of children with RAP is substantially higher than would be expected in the general population. Anxiety appears to be a major concern in this population; children with RAP

not only have higher than average symptoms of anxiety, but their levels of anxiety are severe enough to qualify for a diagnosis in the majority of this sample.

Previous research examining anxiety and other internalizing symptoms in children with RAP has often reported only overall levels of internalizing symptoms without distinguishing between anxiety, somatic, and depressive symptoms that contribute to total internalizing subscales, such as on the CBCL and YSR (e.g., De Los Reyes & Kazdin, 2005). This makes it difficult to determine whether increased levels of internalizing symptoms previously found in children with RAP relate to psychological symptoms or to physical symptoms that are also captured in total internalizing subscales. This study found that the increases in internalizing symptoms previously found in children with RAP are not due to somatic symptoms alone, and that anxiety is also a significant psychological feature of this population.

These data reveal a strong relation between RAP and anxiety in children. Of note is that stomachaches with functional impairment also appear to be associated with anxiety disorders. Children with anxiety in this sample endorsed somatic symptoms as frequently as children with RAP. Nearly one-third of the children with anxiety disorders also met Apley's (1975) criteria for RAP. In addition, 14% of children in the anxiety sample with frequent stomachaches had seen a health provider for their gastrointestinal distress.

Interestingly, data from the CBCL and MASC showed that the mean scores from this sample of children with anxiety and children with RAP did not fall into the clinically significant range based on the normative data for these measures. Although these mean scores were lower than expected, the reliability of the diagnoses based on the parent and child administrations of the K-SADS was excellent. Therefore, this pattern of findings

suggests that the checklists may, at least in the present samples, under predict diagnoses of anxiety. This may be in part a reflection of the heterogeneity of anxiety symptoms included in the checklists relative to the more homogeneous sets of symptoms that are needed to meet criteria for specific anxiety disorders. Further, the clinical cut-offs for these measures are not designed to predict specific diagnoses. For example, the cut-offs for the CBCL were set minimize type I and type II errors in distinguishing children referred for psychological treatment from those not referred for treatment, rather than for a diagnosis of an anxiety disorder.

Association between RAP and Stress Reactivity and Recovery

Physiological stress reactivity and recovery in response to three laboratory-based stressors, as well as self-reported stress reactivity, was also examined. Children with RAP, as compared to children with anxiety disorders and healthy controls, reported that they are significantly more reactive to stress, including increased levels of rumination, intrusive thoughts, emotional arousal, physiological arousal, and impulsive action in response to a social stressor. Self-reported stress reactivity was correlated positively with mean heart rate at all five time points examined in this study (baseline, during the laboratory stressors, and during recovery). Higher heart rates throughout the study also corresponded to increased levels of psychological symptoms and somatic complaints reported by both parents and children. Further, heart rate during the psychological stressors predicted differences in levels of psychological symptoms of anxiety and somatic complaints above and beyond group membership. These results confirm previous research findings that associate self-reported anxiety symptoms with elevated

heart rate (Weems et al., 2005) and indicate that, in general, symptoms of anxiety are associated with higher physiological arousal (Rosenberg & Kagan, 1989; Weems et al., 2005). Importantly, these findings provide support for the hypothesis that stress reactivity, both self-reported and physiological responses to laboratory stressors, is related to both RAP and anxiety in children, and that their responses to stress may be contributing to both somatic and anxiety symptoms.

Children with RAP had a significantly elevated heart rate at baseline compared to healthy controls, and their heart rate remained higher than both the healthy control children and children with anxiety disorders during the laboratory-based stressors and during recovery. This pattern of sympathetic hyperarousal may be indicative of a decreased threshold in response to stress in this population. That is, the laboratory study itself may have served as a stressor for these children, increasing their heart rates at baseline. As the study progressed, the heart rates of the children with RAP did not decrease as they did in the healthy control and anxious children, but remained stably high throughout the study. This pattern of a high and stable resting heart rate is similar to that found in children with behavioral inhibition, a temperamental precursor to anxiety disorders (Kagan, Reznick, & Snidman, 1988). It could be hypothesized, therefore, that this biobehavioral reactivity to stress is a marker of and possibly contributing to the high levels of anxiety found in children with RAP. Combined with their high scores on self-reported stress reactivity, these data indicate a promising avenue for continued research examining responses to stress in children with RAP.

The data examining vagal tone and parasympathetic nervous system functioning did not reveal significant differences between the three groups. This is likely due to this

particular study's difficulties in acquiring this aspects of the psychophysiological data. First, many of the children participating in the study had missing data due to movement artifacts that made it impossible to conduct the spectral analyses needed to extract an index of vagal tone. Despite efforts to keep children still, the study protocol required some movement as the children shifted positions for the psychological stress tasks and, in particular, for the cold pressor. This resulted in electrocardiograms that contained too much noise for further analysis. Second, after extracting the data, it was necessary to further clean the low and high frequency variables to remove outliers. Many of the children had unreliable vagal tone data that were deleted from further analyses². This further increased the number of children missing data that, in turn, significantly reduced the power to detect differences between groups. A third major challenge that confronted the vagal tone data analyses in this study is that the procedure used to conduct the spectral analysis of the electrocardiograms obtained during the laboratory procedure (Fast Fourier Transform) required at least 5 minutes of continuous heart rate data collection. Several of the study time periods were less than 5 minutes, making the FFT and resulting spectral analysis impossible.

Studies have shown that high, stable heart rates across situations including during rest and during stress are indicative of low vagal tone (Beauchaine, 2001). The data presented here show that in this sample of children with RAP, a high, stable heart rate was maintained throughout the study protocol. Though it cannot be definitively determined that in addition to the high heart rate there was concurrent low vagal tone, future research might continue to explore parasympathetic nervous system functioning in

² Data was cleaned after consultation with Andre Diedrich, M.D., Ph.D., who suggested that any value above 5000 Hz/msec² was invalid.

this population. Previous research examining vagal tone in populations of adults and children with anxiety, and in adults with IBS, has shown that low vagal tone is linked to anxiety and somatic symptoms (e.g., Hastings, Sullivan, McShane, Copland, Utendale, & Vyncke, 2008; Lyonfelds, Borkovec, & Thayer 1995). This evidence suggests that the link between RAP and anxiety may lay in parasympathetic dysfunction resulting in a decreased ability to recover from stress. Preexisting biological factors, such as decreased vagal tone, increased sympathetic arousal, impaired parasympathetic recovery from stress, and visceral hypersensitivity, may influence how an individual automatically responds to stress, which in turn may affect how a child copes with stress. This may, in turn, increase their rates of psychological symptoms and decrease their ability to engage with the stressor such that less-functional disengagement strategies are used. Because parasympathetic activation is required for both stress recovery and processes relating to digestion and to reducing overall arousal, it remains a promising avenue of research particularly for distinguishing the mechanisms that are common to or discriminate between RAP and anxiety in children.

Pain Tolerance and Sensitivity

Children with RAP also responded differently to a painful physical task, and pain ratings across the sample were positively correlated with self-reported somatic complaints. Children with RAP reported that the cold pressor was significantly more painful than the children with anxiety and well children despite the fact that they held their arms in the water for approximately the same amount of time. These data indicate that children with RAP experience not only visceral hypersensitivity (as indicated by

their abdominal pain symptoms), but sensitivity to peripheral pain as well. It is also interesting to note that responses to a laboratory based physical stressor correlated positively with child-reports of somatic complaints in general. As an aside, this study also showed that the cold pressor is a reliable method to induce physiological stress in children and adolescents.

Limitations

The present study has several limitations. First, the sample size is relatively small making it difficult to detect effects. Small sample size may have particularly affected the analyses of the child self-report questionnaire data. The YSR was administered to all children 11 years of age or older, which excluded those children in this sample ages 8 to 10. The sample size in each of the three groups dropped nearly by half, thus decreasing power to detect differences between groups. Further, as mentioned above, the psychophysiological data was also greatly reduced due to difficulties with data collection and analyses, also resulting in reduced power.

A second limitation is the difficulty in determining the degree of overlap between RAP and anxiety disorders in this study. This is in part because the samples of RAP and anxiety children were drawn from a tertiary care setting for the treatment of pediatric gastrointestinal problems (RAP group) and from a community mental health center that treats children with anxiety (anxiety group). As a result, children in this study are likely to differ from children in the general population who suffer from RAP or anxiety who have not sought or been referred for medical or psychiatric care. “Berkson’s bias” suggests that it is the confluence of multiple problems or disorders that initiates patients

to seek or be referred for professional care when symptoms arise, increasing the likelihood of comorbid problems in clinical samples (McConaughy & Achenbach, 1994). Since this sample was drawn from a tertiary care clinic, Berkson's bias would predict the comorbidity of RAP and anxiety to be higher in samples presented in this study than would be found in the general population of children with either of these disorders. The degree of overlap between RAP and diagnoses of anxiety disorders may thus be inflated. Despite this concern, data from this study do suggest that children who are treated in tertiary care clinics for their abdominal pain are likely to have symptoms of anxiety.

Further, our well sample was not community-based but rather was selected to include only children without abdominal pain and anxiety to provide a comparison group that was free of the RAP and anxiety disorders. Thus, our comparison group was highly selected and not representative of the general population of children. It should be noted that, despite our selective recruitment process, one child in the well group met criteria for Simple Phobia. Lastly, a requirement for participation in the study in the anxious group was that the child was currently in treatment for an anxiety disorder *or* had received treatment for anxiety in the past. Several of the children in the anxious group had already completed treatment for anxiety, which may have resulted in overall lower levels of anxiety symptoms. This is indicated in the anxious group's scores on the CBCL, YSR, and MASC, where, on average, scores did not reach the clinical range. However, despite this, all of the children in the anxiety group met criteria for an anxiety disorder at the time of the study, thereby making them eligible for participation. Future research might benefit from having an anxiety comparison group that has not undergone treatment for anxiety prior to participation in the study.

These limitations notwithstanding, the present study extends the pediatric literature on psychological and psychophysiological factors involved in chronic pain. The use of multiple methods and multiple informants (child-report, parent-report, use of both questionnaire and diagnostic data, biobehavioral responses to stress) increases reliability in measuring psychological and psychophysiological factors involved in recurrent abdominal pain in children.

Implications

The data presented here show a strong association between RAP and anxiety disorders. Although the degree and nature of this co-occurrence is not fully understood, it could be explained in at least three ways. First, RAP and anxiety may be distinct but comorbid disorders. Because the base rate of RAP is higher in the general population than the base rate of anxiety disorders, it is likely that there are more children with RAP who have comorbid anxiety than the reverse. Further, if RAP and anxiety are distinct disorders, future research is needed to determine if there is temporal precedence for either RAP or anxiety disorders.

A second possibility is that RAP may be a subtype of an anxiety disorder. Given that, in this study, children with RAP had increased levels of anxiety symptoms and most children with RAP also met criteria for an anxiety disorder, in addition to the fact that many children with anxiety disorders also presented with stomachaches, it is possible that the presence of persistent and significant abdominal pain is a distinguishing feature of a distinct subtype of anxiety.

Third, it is important to note that RAP is characterized by a single symptom—abdominal pain. Therefore, rather than a separate disorder, RAP may be a salient and significant symptom of broader anxiety syndromes or disorders. The strong association between abdominal pain and other symptoms of anxiety may reflect the centrality of abdominal pain as a key symptom of anxiety. In support of this, abdominal pain and stomachaches are criteria for two anxiety disorders in the DSM-IV: Separation Anxiety Disorder (SAD) and Generalized Anxiety Disorder (GAD). Though not every child who meets criteria for these two disorders has abdominal pain symptoms, abdominal pain and other somatic complaints remain diagnostic features of SAD and GAD. And, in this sample as well as other samples of children with anxiety disorders, many children with anxiety also report stomachaches significant enough to disrupt everyday functioning.

Future Directions for Research

The association between RAP and anxiety symptoms and disorders is of potentially great clinical and research importance. Oftentimes, psychosocial problems are not addressed in primary or tertiary care pediatric clinics. However, as findings from this study suggest, psychosocial concerns are not only present in children with RAP, they may also contribute to the exacerbation or maintenance of the disorder. Important goals of pediatric health care professionals who treat children with RAP are to reduce the number of pain episodes and frequency of medical exams and visits, ease the burden on the medical community, and increase the quality of life in these children. Using a biopsychosocial approach when assessing and treating RAP in children could lead to interventions with children with RAP and their caregivers targeting stress, coping and

anxiety. Understanding RAP as associated with underlying anxiety disorders may facilitate referral for psychiatric evaluation and treatment. In cases where anxiety disorders are suspected or are present, or when the family or child is experiencing a large amount of stress and reduced emotional resources, mental health referrals may be warranted.

Results from this study indicate that further research examining the role of temperament, stress, stress reactivity, anxiety, and coping in recurrent episodes of abdominal pain in children is necessary. The number of studies examining psychosocial correlates of RAP is growing; however, several questions that could have direct beneficial effects for this population need to be addressed.

- 1) Understanding the association between RAP and anxiety. Results of this study and previous studies examining psychological symptoms in children with RAP have shown that children with RAP and their parents often endorse high levels of internalizing symptoms, particularly symptoms of anxiety. Continued research using both questionnaires and diagnostic interviews to assess symptoms and diagnoses of psychopathology are needed in order to further delineate this association. Psychopathology, including anxiety and depression, can be conceptualized and measured both dimensionally and categorically. As a consequence, the use of checklists and diagnostic interviews are both relevant in research on the co-occurrence of anxiety and depression with RAP. Diagnostic interviews permit researchers to understand not only the level of symptoms in their sample, but also allow distinctions among specific types of disorders.

Certain anxiety disorders, such as separation anxiety disorder, generalized anxiety disorder, or social phobia, may be more prevalent than other types of anxiety in this population. Future research should continue to measure psychopathology using both dimensional and categorical methods in order to make these important diagnostic distinctions. Further, and perhaps most importantly, use of community-based samples will help overcome Berkson's bias and give a better representation of RAP and anxiety in the general population.

- 2) Compare children with RAP to children with an organic cause for their abdominal pain. Children who receive a functional diagnosis for their abdominal pain, such as RAP, may differ on levels of both somatic and psychological symptoms when compared to children who have an organic cause for their abdominal pain. To date, few studies have directly compared these two groups.
- 3) Further research exploring temperament in children with RAP and anxiety. There are minimal data on temperament in children with RAP. However, heart rate and stress reactivity and recovery data from this study suggest that temperament may play a role in the development and course of RAP in children. Temperament may be measured by using direct observations of behavior or questionnaire data, typically obtained from parents. Both sources of information are important, however observational data may provide a better assessment of temperamental characteristics in children, as observations are not subject to potential biases in parents' reports on their children's temperament. Application of these two methodologies to populations of children with RAP and anxiety would provide

important information that could lead to identification of factors that put children at risk for developing RAP in later childhood.

4) Examine how children with RAP and anxiety respond to and recover from stress.

This study explored the potential biological and psychological underpinnings of RAP in children, including possible autonomic nervous system irregularities that may contribute to both episodes of pain and anxiety in children with RAP.

Similar to research examining temperament in children with RAP and anxiety, research looking at stress reactivity and recovery in this population is sparse.

Further research examining stress reactivity, stress recovery, and coping is needed in order to help elucidate these connections, and will provide useful clues into the development and progression of RAP.

5) Continued research on coping in children with RAP and anxiety. This study

found an association between the manner in which a child with RAP copes with stress and functional and psychological outcomes. Future studies examining coping in this population are necessary in order to delineate whether the way in which children with RAP copes with their episodes of abdominal pain, as detailed by Thomsen et al. (2002), Walker et al. (1997), and Compas et al. (2006) is similar to the way in which they cope with other forms of stress. Comparison of the ways that children with RAP and children with anxiety disorders cope with common sources of stress (e.g., school achievement stress or peer stress) will help identify similarities in the coping strategies used by these two groups of children.

6) Focus on treatment outcome studies of psychological interventions for children with RAP and anxiety. As detailed above, the way children cope with their

episodes of abdominal pain contributes significantly to both the exacerbation and recurrence of pain symptoms, as well as the incidence of internalizing symptoms. Further, the strong correlation between RAP and anxiety indicates that treatment of anxiety may also induce a reduction of RAP symptoms. There is extensive literature showing that teaching cognitive-behavioral skills and strategies to children with anxiety disorders is ameliorative (Kendall et al., 1997). Application of these treatment protocols to a population of children with RAP could be of great benefit.

- 7) Explore the developmental course of RAP in children. The evidence presented in this study shows a strong association between RAP and anxiety in children. However, this study was not able to determine the developmental course of RAP in children. Longitudinal studies would help to elucidate whether anxiety precedes, appears at the same time, or follows the incidence of RAP symptoms, which could ultimately inform medical and psychological interventions.
- 8) Increase statistical power by recruiting larger samples in research examining children with RAP. The current study was underpowered due to small sample sizes in each of the three groups. This limited the ability to detect differences between children with RAP and controls that were small to medium in magnitude. As a result, this study may have underestimated the degree to which children with RAP may differ from healthy controls. Further, small sample size reduced power to detect important individual differences, such as differences in symptomatology between gender and age. Because examination of differences as function of individual difference factors requires the creation of subgroups, larger samples are

needed to generate sufficiently large subgroups to detect differences as a function of the grouping variables. Larger groups will also make it possible to detect differences in psychophysiological data, particularly data relating to vagal tone.

Conclusions

Recurrent abdominal pain (RAP) is the most common type of recurrent pediatric pain, experienced by 8% to 25% of school-aged children (Apley, 1975; Colletti, 1998; McGrath, 1990). Much evidence shows that this condition adversely affects many areas of a child's functioning, including repeated school problems and absences (Robinson, Alvarez, & Dodge, 1990) and frequent visits to pediatricians (Starfield, Katz, & Gabriel, 1984). Two striking features of RAP are the degree of comorbidity between RAP and anxiety, and the precipitating role that stress plays in predicting episodes of both RAP and anxiety. The central clinical implication of the current study is that a large subset of children with RAP also has comorbid anxiety and other internalizing symptoms. In addition, children with RAP demonstrate increased levels of stress reactivity and psychophysiological arousal. Further understanding of the links between RAP, stress, and anxiety is essential to understanding the development and progression of RAP, and in informing the prevention and treatment of the disorder.

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