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OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

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*Pediatrics* 2004;113;817-824

DOI: 10.1542/peds.113.4.817

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<http://www.pediatrics.org/cgi/content/full/113/4/817>

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# Recurrent Abdominal Pain, Anxiety, and Depression in Primary Care

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**ABSTRACT.** *Objective.* The prevalence of psychiatric disorder in children and adolescents with functional recurrent abdominal pain (RAP) is unknown. Our aim was to determine whether RAP is associated with psychiatric symptoms and disorders, anxious temperament, and functional impairment in pediatric primary care.

*Methods.* Children and adolescents who were 8 to 15 years of age, inclusive, and presented with RAP ( $N = 42$ ) or for routine care in the absence of recurrent pain ( $N = 38$ ) were identified by a screening procedure in pediatric primary care office waiting rooms and recruited to participate in a case-control study. Outcome measures were psychiatric diagnoses generated by standardized psychiatric interview administered blind to subject status and self, parent, and clinician ratings of child psychiatric symptoms, temperamental traits, and functional status.

*Results.* RAP patients were significantly more likely to receive a diagnosis of a psychiatric disorder, with a categorical anxiety disorder in 33 (79%) and a depressive disorder in 18 patients (43%), and higher levels of anxiety and depressive symptoms, temperamental harm avoidance, and functional impairment than control subjects. Anxiety disorders (mean age of onset: 6.25 [standard deviation: 2.17] years) were significantly more likely to precede RAP (mean age of onset: 9.17 [standard deviation: 2.75] years) in patients with associated anxiety.

*Conclusions.* Youths who present with RAP in primary care deserve careful assessment for anxiety and depressive disorders. Future studies should examine treatments that are proved to be efficacious for pediatric anxiety and/or depressive disorders as potential interventions for RAP. Longitudinal, family, and psychobiological studies are needed to illuminate the nature of observed associations among RAP, anxiety, and depression. *Pediatrics* 2004;113:817–824; *abdominal pain, anxiety, depression, functional colonic diseases, primary care.*

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ABBREVIATIONS. RAP, recurrent abdominal pain; RA, research assistant; K-SADS-PL, Schedule for Affective Disorders and Schizophrenia for School Age Children, Present and Lifetime Version; CBCL, Child Behavior Checklist; FET, Fisher exact test; SD, standard deviation; TCA, tricyclic antidepressant.

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Received for publication May 19, 2003; accepted Sep 10, 2003.

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Pediatric recurrent abdominal pain (RAP) has been defined as at least 3 episodes of abdominal pain that occur over a period of at least 3 months and are severe enough to affect the activities of the child.<sup>1,2</sup> RAP is common, affecting between 7% and 25% of children and adolescents in available school-based or community samples<sup>1,3–12</sup> and accounts for 2% to 4% of pediatric office visits.<sup>13</sup> Approximately 8% of middle and high school students in a community-based study reported seeing a physician for abdominal pain that year.<sup>9</sup> Prevalence of RAP increases with age into adolescence,<sup>1,5,9,11</sup> and age and gender interact, with an equal gender ratio in early childhood,<sup>7,12</sup> and symptom reporting by girls predominating by late childhood.<sup>1,11</sup> Lower socioeconomic status has been associated with RAP in some studies<sup>4,14,15</sup> but not others,<sup>12</sup> and the impact of race and ethnicity has not been well studied.

Explanatory physical disease cannot be identified in the overwhelming majority of children with RAP, particularly in the absence of "red flags" such as weight loss, gastrointestinal bleeding, systemic symptoms (eg, fever), laboratory evidence of anemia or inflammation, persistent vomiting, or pain that frequently awakens the child at night.<sup>16–19</sup> *Helicobacter pylori* infection<sup>20,21</sup> and celiac disease<sup>22</sup> are not etiologic in most cases, and despite suspicions about food allergies, lack of dietary fiber,<sup>23</sup> gluten sensitivity, and lactose malabsorption,<sup>24</sup> results of dietary intervention such as fiber supplementation and lactose-free diets have been disappointing.<sup>25</sup> Consequently, symptom-based criteria for "functional gastrointestinal disorders" in children have been developed and classify affected children on the basis of the perceived location of the discomfort and any associated changes in bowel patterns.<sup>26</sup>

The lack of a clear-cut biomedical explanation sufficient to account for the pain and disability in most affected children led early workers to propose that RAP was most often a "psychosocial" disorder,<sup>1,27,28</sup> and the importance of a "biopsychosocial" approach to diagnosis and management has been emphasized.<sup>29</sup> RAP has been associated with school absenteeism and perceived health limitations,<sup>9,15,30–32</sup> and with few exceptions<sup>33,34</sup> has been associated with an excess of anxiety and/or depressive symptoms in studies comparing affected with unaffected youths in clinically referred<sup>15,30–32,35</sup> and community-based samples.<sup>7,9,12,36</sup> Despite the prevailing beliefs of many parents,<sup>37</sup> pediatricians, and gastroenterologists that psychosocial factors are of relevance in

youths with RAP,<sup>29</sup> only 2 controlled studies have examined the prevalence of psychiatric disorders using research interviews, with both documenting high rates of psychiatric disorder in children with RAP in specialty care.<sup>30,35</sup> The relationship between RAP and psychiatric disorder is poorly understood, particularly in primary care, where recognition of psychiatric disorder and mental health referral rates have been reported to be low.<sup>38</sup> Little is known about the temporal relationship between RAP and symptoms of anxiety and depression, with popular beliefs that the emotional distress commonly observed in children with RAP is caused by the pain being purely speculative. In addition, although children with RAP have been described as temperamentally anxious or inhibited,<sup>1,2,39</sup> studies using standardized measures comparing affected with unaffected children have not been accomplished.

We report the initial results of a case-control study comparing children and adolescents who presented with RAP in primary care with pain-free control subjects who presented with minor illness or for well-child care. We hypothesized that patients with RAP would be significantly more likely than control subjects to meet diagnostic criteria for anxiety and depressive disorders and to report higher levels of anxiety and depressive symptoms, anxious temperament, and functional impairment.

## METHODS

### Participants

A consecutive sample of 42 children and adolescents with functional RAP and 38 pain-free comparison subjects aged 8 to 15 years, inclusive, and living with at least 1 biological parent were recruited by an office-based screening procedure during a 2-year period from primary care pediatric practices in western Pennsylvania affiliated with Children's Community Pediatrics and the Children's Hospital of Pittsburgh. These included 2 urban practices (each serving approximately 9000 children and employing 7 pediatricians), 2 suburban practices (each serving approximately 7000 children and employing 5 or 6 pediatricians), and 1 rural practice (serving approximately 10 000 children and employing 10 pediatricians). Children with RAP were required to have experienced 3 or more episodes of abdominal pain sufficient to interfere with activities or function in the previous 3 months. Comparison subjects were free of RAP, headache, chest pain, and limb pain in the previous 3 months. Children who had physical disease considered sufficient to explain the child's RAP symptoms or a non-gastrointestinal serious chronic physical disease (eg, epilepsy, diabetes) were excluded. Children who had RAP and exhibited "atypical" symptoms or findings considered indicative of explanatory physical disease were also excluded.<sup>16</sup> Such "atypical" findings included persistent nighttime awakenings as a result of abdominal pain (>3 per month); abnormal abdominal or rectal examination; history of rectal bleeding, Hematest-positive stool, or hematemesis; persistent or bilious vomiting; involuntary weight loss or growth deceleration; abdominal pain exclusively associated with menstruation; fever; dysuria; and available laboratory evidence suggesting explanatory physical disease (eg, elevated erythrocyte sedimentation rate, anemia, abnormal liver function tests). Other exclusionary criteria included pregnancy and mental retardation.

### Procedure

The Human Rights Committee of the Children's Hospital of Pittsburgh approved the study. Children who presented for routine pediatric care and their parents were introduced to the study in the primary care practice waiting area via a brief letter of introduction. Parents who were willing to participate then completed a visit questionnaire assessing whether abdominal pain

was a reason for the visit and whether the child had any history of recurrent pain in the past 3 months, as well as an abbreviated version of the Pediatric Symptom Checklist,<sup>40,41</sup> a screen for common emotional and behavioral problems. A research assistant (RA) reviewed the questionnaire and identified children who presented with RAP as a reason for the visit. Physician referrals were not accepted to minimize the possibility of referral bias. Whenever a patient with RAP was identified, 3 potential control subjects of the same age and gender and presenting for minor illnesses or well-child care within the practice of origin and with no history of recurrent pain were identified from visit questionnaires collected sequentially after the RAP patient.

Potential RAP patients and pain-free control subjects were contacted by the RA and invited to participate in the full research assessment. Informed consent was obtained at the initial interview. The RA confirmed criteria for eligibility and collected demographic information, physical health history, and parent and child self-report measures and checked for missing data. The medical record was reviewed, and the child's primary care physician was contacted when appropriate to clarify whether the presenting symptoms were truly medically unexplained or functional. The psychiatric research interviewer (J.C.) was blind to subject status and interviewed the parent(s) first, then the child alone, followed by meeting with parent(s) and child if any areas of discrepancy were identified. Questions related to somatic symptoms were omitted from the psychiatric interview assessment, a single 1.5- to 3-hour session with breaks as needed. Children and parents who completed the full assessment were compensated for participation.

## Observations and Measurements

### Sample Characteristics

Demographic information included age, race, gender, religion, school placement, and socioeconomic status as derived from the Four-Factor Hollingshead Scale.<sup>42</sup> Pubertal development was assessed using the Petersen Pubertal Development Scale,<sup>43</sup> a self-report questionnaire with adequate reliability and validity against physical examination.

### Psychiatric Disorder

Schedule for Affective Disorders and Schizophrenia for School Age Children, Present and Lifetime Version (K-SADS-PL)<sup>44</sup> is a semistructured interview designed to determine present episode and lifetime history of psychiatric disorder. The K-SADS-PL also collects information regarding psychiatric treatment history. Interrater and test-retest reliability and convergent and discriminant validity have been established.

### Psychiatric Symptomatology

Child Behavior Checklist (CBCL)<sup>45</sup> is a well-established parent-report questionnaire with excellent psychometric properties that provides a global measure of psychopathologic symptoms in children and adolescents, generating a total problem score and internalizing and externalizing symptom scores.

Children's Depression Inventory<sup>46</sup> is a self-report inventory of depressive symptoms in children and adolescents with good test-retest reliability and concurrent validity.

Screen for Child Anxiety Related Emotional Disorders<sup>47</sup> is a 41-item self-report questionnaire that has good internal consistency, test-retest reliability, and concurrent validity with psychiatric interview. There are child and parent proxy report versions. Symptom severity is rated over the previous 3 months on a 0- to 2-point rating scale. Factor analysis generated a 5-factor solution for both the parent and the child versions that conceptually match panic/somatic anxiety, generalized anxiety, separation anxiety, social phobia, and school phobia. Questions 2 and 11 ask about somatic pain during emotional distress and load on the school phobia subscale; responses to questions 2 and 11 were dropped from analyses comparing RAP patients with control subjects.

Pediatric Symptom Checklist-17<sup>40</sup> is a 17-item abbreviated version of the original 35-item parent-completed scale<sup>41</sup> developed as a screen for symptoms of emotional and behavioral disorders in pediatric settings and generates internalizing, externalizing, and attentional subscales.

## Temperament and Character

Junior Temperament and Character Inventory<sup>48</sup> is a 105-item self-report pediatric adaptation of the well-validated and reliable Temperament and Character Inventory<sup>49</sup> and assesses 4 temperamental (Novelty Seeking, Harm Avoidance, Reward Dependence, and Persistence) and 3 character traits (Self-Directedness, Cooperativeness, and Self-Transcendence) using a true-false format. Cloninger's unified biosocial theory of personality conceptualizes personality as a combination of heritable, neurobiologically based temperamental traits and character traits rooted in social learning.<sup>50</sup> The Junior Temperament and Character Inventory has moderate reliability on self-report and good agreement with parent and teacher reports, with preliminary support for its validity in youths.<sup>48</sup>

## Functional Status

Children's Global Assessment Scale<sup>51</sup> is a reliable and valid interviewer assessment of child and adolescent functioning. Columbia Impairment Scale<sup>52</sup> is a parent-completed global measure of psychosocial impairment with high internal consistency, excellent test-retest reliability, and good validity. Functional Disability Inventory<sup>53</sup> assesses the child's functional disability as a result of physical health status in the previous 2 weeks, with high levels of internal consistency and demonstrated reliability.

## Statistical Analyses

Data from the assessments were collected using scannable forms, then scanned, verified, and stored by the RA under the supervision of the database administrator, who checked for missing data or outlying values. The appropriate parametric or non-parametric test was used for each outcome. RAP patients and control subjects were compared on demographic and other potentially confounding variables using the appropriate univariate tests, and variables associated with differences related to the outcomes in question were treated as covariates subsequent to univariate analyses. We compared the proportion of patients with control subjects with psychiatric diagnoses generated by the K-SADS-PL using the standard test for proportions, with categorical data being compared using the  $\chi^2$  test or Fisher exact test (FET) as appropriate. Continuous data were examined using the appropriate *t* test or Mann Whitney *U* test. Effect sizes were calculated using Cohen *d* for continuous data and  $\omega$  for categorical data.

## RESULTS

### Sample Characteristics

The study sample of 42 RAP patients and 38 control subjects had a mean age of 11.8 years (standard deviation [SD]: 2.29) and was 77% white and 57% female. Enrolled patients and control subjects did not differ with regard to age, gender, race/ethnicity, socioeconomic status, birth weight, gestational age at birth, or level of pubertal development (Table 1). RAP patients were significantly more likely than control subjects to live in single-parent families (31% vs 11%;  $\chi^2 = 4.97$ ,  $P = .03$ ) and in "nonintact" families with only 1 biological parent (52% vs 18%;  $\chi^2 = 9.96$ ,  $P = .002$ ). A total of 1260 children and adolescents were screened in primary care, identifying 67

eligible RAP patients (5.3%). Of these, 42 (63%) RAP patients enrolled and completed the full research assessment. The 12 (17.9%) potential patients who declined participation and the 13 (19.4%) whom we were unable to contact did not differ from enrolled RAP patients with regard to demographics or psychopathologic symptoms on the Pediatric Symptom Checklist-17, with the only exception being that those who refused to participate were significantly more likely to be white than enrolled patients (100% vs 71%;  $P = .046$ , FET).

## Psychiatric Disorder

### Anxiety and Depressive Disorders

Patients and control subjects were evaluated for current and lifetime psychiatric disorders using the KSADS-PL. A current anxiety disorder was identified in 33 (79%) of the 42 RAP patients, with separation anxiety disorder in 18 (43%), generalized anxiety disorder in 13 (31%), and social phobia in 9 patients (21%). A depressive disorder was diagnosed in 18 (43%) of 42 children with RAP, with major depressive disorder in 13 (31%), dysthymic disorder in 4 (10%), and a subthreshold depressive disorder (depressive disorder not otherwise specified) in 3 (7%). In total, 81% of RAP patients met criteria for an anxiety or depressive disorder. With only 1 exception, all RAP patients with depressive disorders also experienced an associated anxiety disorder. Although children younger than 12 years were significantly more likely to have a diagnosis of an anxiety or a depressive disorder in our sample than subjects 12 years of age and older (64% vs 32%;  $\chi^2 = 8.54$ ,  $P = .003$ ), age had no impact on the observed relationship between RAP patients and control subjects; differences between the groups remained significant when the data were stratified by age (89% vs 25% for children under age 12;  $\chi^2 = 17.37$ ,  $P < .001$ ; 69% vs 5% for children 12 and older;  $\chi^2 = 17.67$ ,  $P < .001$ ). Significant differences related to gender or race were not observed (Table 2).

### Disruptive Behavior Disorders

RAP patients were significantly more likely than control subjects to experience any disruptive behavior disorder, although case-control differences were less extreme than those observed for anxiety and depressive disorders. Differences between patients and control subjects with regard to specific disruptive behavioral disorders were not observed, but there was a trend suggesting that children with RAP are more likely to meet criteria for oppositional de-

TABLE 1. Initial Characteristics of RAP Patients and Control Subjects

	RAP (n = 42)	Controls (n = 38)	Statistic	p Value
Female gender, %	24 (57.1)	22 (57.9)	$\chi^2$	NS
Race, % white	32 (76.2)	30 (78.9)	$\chi^2$	NS
Age (mean [SD])	11.4 (2.2)	12.3 (2.3)	<i>t</i>	NS
SES (mean [SD])	2.4 (1.2)	2.2 (1.1)	MWU	NS
Pubertal level, boys	11.1 (3.0)	10.6 (2.8)	<i>t</i>	NS
Pubertal level, girls	12.8 (3.6)	13.6 (3.6)	<i>t</i>	NS

SES indicates socioeconomic status; MWU, Mann Whitney *U* test; NS, not significant.

**TABLE 2.** Current Psychiatric Diagnoses by KSADS-PL

	RAP % (n = 42)	Controls % (n = 38)	Statistic	P Value	Effect Size*
Any anxiety disorder†	78.6	10.5	$\chi^2 = 37.16$	<.001	.68
Separation anxiety	42.9	2.6	$\chi^2 = 17.83$	<.001	.47
GAD	31.0	0	$\chi^2 = 14.04$	<.001	.42
Social phobia	21.4	0	FET	.003	.34
Simple phobia	19.0	7.9	$\chi^2 = 2.09$	.15	.16
Panic disorder	2.4	0	FET	1.0	.11
OCD	2.4	0	FET	1.0	.11
PTSD	4.9	0	FET	.49	.16
Any depressive disorder†	42.9	7.9	$\chi^2 = 12.60$	<.001	.40
MDD	31.0	2.6	$\chi^2 = 11.08$	.001	.37
Dysthymia	9.5	2.6	FET	.36	.14
Depressive disorder NOS	7.1	2.6	FET	.62	.10
Any emotional disorder†	81.0	13.2	$\chi^2 = 36.7$	<.001	.68
Any disruptive disorder†	23.8	7.9	$\chi^2 = 3.71$	.05	.22
ADHD	14.3	7.9	FET	.49	.10
Inattentive	11.9	2.6	FET	.20	.18
Hyperactive-impulsive	2.4	0	FET	1.0	.11
Combined	0	5.3	FET	.22	.17
ODD	19.0	5.3	FET	.09	.21
Conduct disorder	0	0			

GAD indicates generalized anxiety disorder; OCD, obsessive compulsive disorder; PTSD, posttraumatic stress disorder; MDD, major depressive disorder; NOS, not otherwise specified; ADHD, attention-deficit/hyperactivity disorder; ODD, oppositional defiant disorder.

\*  $\omega$ .

† Does not include adjustment disorders.

fiant disorder (19% vs 5.3%;  $P = .09$ , FET). Age, gender, and race did not influence the diagnosis of disruptive behavior disorders, although there was a trend for minority subjects to be diagnosed at a higher rate (33% vs 11%;  $P = .06$ , FET).

#### Other Disorders

The groups did not differ with regard to the presence of adjustment disorders, tic disorders, or elimination disorders, and no children with bipolar disorder, psychosis, eating disorders, or alcohol or substance abuse/dependence were identified in either group.

#### Psychiatric Treatment History

RAP patients were significantly more likely to report a history of outpatient psychiatric treatment (45.2% vs 21.1%;  $\chi^2 = 5.22$ ,  $P = .02$ ) than control subjects but did not differ with regard to current or past history of psychoactive medication use (16.7% vs 13.2%;  $\chi^2 = 0.193$ ,  $P = .66$ ). Specific medications used by RAP patients or control subjects were antidepressants (7.1% vs 5.3%;  $P = 1.0$ , FET) and stimulants (9.5% vs 13.2%;  $P = .73$ , FET), with use of antipsychotics, sedatives, and mood stabilizers being denied by all study participants. One RAP patient reported a history of inpatient psychiatric hospitalization.

#### Age of Onset

Age of onset for psychiatric disorders was collected independent of that for RAP by different examiners who were blind to the other's finding before coding. Mean age of onset was 9.17 years (SD: 2.75) for RAP, 6.25 years (SD: 2.17) for first definite anxiety disorder, and 9.5 years (SD: 3.0) for first definite depressive disorder in patients with comorbid anxiety or depressive disorders. Of the 33 RAP patients

with an anxiety disorder, the anxiety disorder preceded the onset of RAP in 26 (79%) patients and developed coincidentally (within 1 month of RAP onset) in 3 (9%) patients. Anxiety disorder was significantly more likely to precede the onset of RAP, developing a mean of 35.2 months (SD: 34.5) beforehand ( $t = -5.86$ ,  $P < .001$ ). When the 18 RAP patients with comorbid depressive disorder were examined, RAP preceded the development of depressive disorder in 4 (22%) patients, coincided with the onset of depressive disorder within 1 month in 7 (39%) patients, and developed afterward in 7 (39%) patients. Ages of onset for RAP and depressive disorder did not differ ( $t = -0.071$ ,  $P = .94$ ).

#### Psychiatric Symptoms

##### Anxiety Symptoms

RAP patients were significantly more likely than control subjects to exhibit higher levels of anxiety symptoms, regardless of whether symptoms were reported by the child or a parent, and with large effect sizes. RAP patients scored significantly higher than control subjects on all Screen for Child Anxiety Related Emotional Disorders subscales by parent report and all but 1 using child report. Differences remained highly significant when responses to questions about pain were not included in the analyses (Table 3).

##### Depressive Symptoms

RAP patients reported significantly higher levels of depressive symptoms on the Children's Depression Inventory than control subjects, with a correspondingly large effect size (Table 3).

##### CBCL

The CBCL was included as a well-established global measure of parent-reported child psycho-

**TABLE 3.** Anxiety and Depressive Symptoms

Scales (Mean [SD])	RAP ( <i>n</i> = 42)	Control ( <i>n</i> = 38)	Statistic	<i>P</i> Value	Effect Size*
SCARED-Parent	21.1 (14.1)	5.9 (6.1)	<i>t</i> = 6.19	<.001	1.40
SCARED-Parent†	19.2 (13.8)	5.4 (6.0)	<i>t</i> = 5.71	<.001	1.30
Panic anxiety	2.1 (3.0)	0.37 (0.82)	MWU	.002	.79
General anxiety	7.0 (5.0)	1.5 (2.2)	MWU	<.001	1.42
Separation anxiety	3.9 (3.7)	1.0 (1.7)	MWU	<.001	1.01
Social phobia	5.1 (3.8)	2.4 (2.6)	MWU	.001	.83
School phobia	3.0 (2.0)	0.53 (0.89)	MWU	<.001	1.60
School phobia†	1.0 (1.4)	0.08 (0.36)	MWU	<.001	.93
SCARED-Child	19.6 (15.2)	10.4 (9.1)	<i>t</i> = 3.24	.002	.73
SCARED-Child†	17.4 (14.6)	9.6 (9.1)	<i>t</i> = 2.85	.006	.64
Panic anxiety	3.1 (4.0)	1.5 (2.2)	MWU	.03	.50
General anxiety	5.4 (4.9)	2.4 (3.0)	MWU	.008	.74
Separation anxiety	3.9 (3.9)	2.0 (2.2)	MWU	.04	.60
Social phobia	4.5 (4.1)	3.5 (3.3)	MWU	.37	.27
School phobia	2.4 (1.8)	1.0 (0.96)	MWU	<.001	.97
School phobia†	0.57 (1.0)	0.21 (0.66)	MWU	.02	.42
CDI	9.4 (7.5)	4.2 (4.1)	<i>t</i> = 3.80	<.001	.86

SCARED indicates Screen for Child Anxiety Related Emotional Disorders; CDI, Children's Depression Inventory.

\* Cohen *d*.

† Questions 2 and 11 deleted.

pathologic symptoms. We report CBCL findings using mean T scores. CBCL T scores are standardized scores with a mean of 50 and an SD of 10 on the basis of a normative national sample of children who had not been referred for mental health services in the previous year, thus providing a common basis for comparison of RAP patients and control subjects with one another and with a normative sample of children. RAP patients scored significantly higher than control subjects with regard to Internalizing (61.6 [SD: 9.8] vs 43.5 [SD: 8.7]; *t* = 8.24, *P* < .001, *d* = 1.95), Externalizing (50.0 [SD: 9.1] vs 42.8 [SD 8.1]; *t* = 3.49, *P* = .001, *d* = .84), and Total Problems scores (56.1 [SD: 9.2] vs 41.9 [SD: 9.4]; *t* = 6.44, *P* < .001, *d* = 1.53). Significant differences between patients and control subjects with large effect sizes were also noted on the Anxious/Depressed (59.0 [SD: 8.3] vs 51.2 [SD: 3.6]; *t* = 5.15, *P* < .001, *d* = 1.23) and Withdrawn (57.1 [SD: 7.5] vs 50.9 [SD: 2.6]; *t* = 4.73, *P* < .001, *d* = 1.10) scales of the CBCL (Table 4).

### Temperament and Character

RAP patients reported significantly higher levels of temperamental Harm Avoidance than control subjects (9.2 [SD: 4.6] vs 5.6 [SD: 3.2]; *t* = 3.98, *P* < .001), with a relatively large effect size (*d* = .91). There was a trend suggesting lower levels of Self-Directedness in RAP patients (14.7 [SD: 3.8] vs 16.1 [SD: 3.0]; *t* = -1.80, *P* = .08, *d* = .41), but other significant differences were not noted (Table 5).

### Functional Status

The functional status of RAP patients was consistently rated lower than that of control subjects regardless of whether global, physical, or psychosocial functioning was considered and regardless of whether the rating was made by the researcher (Children's Global Assessment Scale), the parent (Columbia Impairment Scale, Functional Disability Inventory-Parent, CBCL Total Competence), or the child (Functional Disability Inventory-Child; Table 6).

**TABLE 4.** CBCL T Scores

CBCL T scores (Mean [SD])	RAP ( <i>n</i> = 42)	Control ( <i>n</i> = 38)	Statistic	<i>P</i> Value	Effect Size*
Total Problem Score	56.1 (9.2)	41.9 (9.4)	<i>t</i> = 6.44	<.001	1.53
Externalizing Score	50.0 (9.1)	42.8 (8.1)	<i>t</i> = 3.49	.001	.84
Internalizing Score	61.6 (9.8)	43.5 (8.7)	<i>t</i> = 8.24	<.001	1.95
Activities Scale	46.3 (6.7)	47.3 (7.1)	<i>t</i> = -0.60	.55	.14
Social Scale	42.1 (7.7)	47.1 (6.9)	<i>t</i> = -2.94	.004	.68
School Scale	45.6 (7.5)	47.8 (8.7)	<i>t</i> = -1.13	.26	.27
Total Competence	42.9 (7.0)	48.3 (8.1)	<i>t</i> = -2.94	.004	.71
Withdrawn Scale	57.1 (7.5)	50.9 (2.6)	<i>t</i> = 4.73	<.001	1.10
Somatic Complaints	68.5 (9.1)	53.8 (4.8)	<i>t</i> = 8.59	<.001	2.02
Anxious/Depressed	59.0 (8.3)	51.2 (3.6)	<i>t</i> = 5.15	<.001	1.23
Social Problems Scale	54.9 (7.3)	51.7 (4.2)	<i>t</i> = 2.32	.02	.54
Thought Problems	53.7 (6.8)	50.7 (2.2)	<i>t</i> = 2.56	.01	.60
Attention Problems	55.1 (7.5)	51.1 (3.8)	<i>t</i> = 2.79	.007	.67
Delinquent Behavior	53.7 (4.5)	50.9 (2.3)	<i>t</i> = 3.38	.001	.78
Aggressive Behavior	53.5 (5.7)	51.1 (3.1)	<i>t</i> = 2.25	.03	.52
Sex Problems Scale	52.6 (5.7)	50.0 (0)	<i>t</i> = 2.16	.08	.65

\* Cohen *d*.

**TABLE 5.** Junior Temperament and Character Inventory

Scales (Mean [SD])	RAP ( <i>n</i> = 42)	Control ( <i>n</i> = 38)	Statistic	<i>P</i> Value	Effect Size*
Novelty Seeking	6.9 (3.2)	7.6 (3.6)	<i>t</i> = .95	.34	.21
Harm Avoidance	9.2 (4.6)	5.6 (3.2)	<i>t</i> = 3.98	<.001	.91
Reward Dependence	4.7 (1.8)	5.2 (2.3)	<i>t</i> = −.87	.39	.24
Persistence	3.2 (1.5)	3.8 (1.6)	<i>t</i> = −1.52	.13	.39
Self-Directedness	14.7 (3.8)	16.1 (3.0)	<i>t</i> = −1.80	.08	.41
Cooperativeness	16.0 (4.3)	16.3 (3.2)	<i>t</i> = −.30	.76	.08
Fantasy (ST 1)	1.4 (1.4)	1.2 (1.2)	<i>t</i> = .50	.62	.15
Spirituality (ST 2 and 3)	3.0 (1.2)	2.9 (1.3)	<i>t</i> = .20	.84	.08

\* Cohen *d*.**TABLE 6.** Functional Status

Scales (Mean [SD])	RAP ( <i>n</i> = 42)	Control ( <i>n</i> = 38)	Statistic	<i>P</i> Value	Effect Size*
CGAS	64.3 (11.0)	85.2 (12.2)	<i>t</i> = −8.06	<.001	1.80
FDI-C	6.5 (6.3)	2.3 (4.1)	<i>t</i> = 3.43	.001	.79
FDI-P	5.4 (5.9)	0.6 (1.3)	<i>t</i> = 5.03	<.001	1.12
CIS	10.7 (5.7)	4.0 (4.8)	<i>t</i> = 5.52	<.001	1.27

CGAS indicates Children's Global Assessment Scale; FDI-C, Functional Disability Inventory—Child; FDI-P, Functional Disability Inventory—Parent; CIS, Columbia Impairment Scale.

\* Cohen *d*.

## DISCUSSION

Pediatric RAP is a significant public health problem and is commonly associated with functional impairment and with anxiety and depressive disorders in primary care. Primary care physicians can expect that approximately 80% of children who present with functional RAP will have an anxiety disorder and that ~40% will meet criteria for a depressive disorder. Study results complement and expand existing literature documenting an excess of anxiety and depressive symptoms in children with RAP in the community<sup>7,9,12,36</sup> and in specialty medical settings,<sup>15,30–32,35</sup> and are very much in keeping with those of Garber et al,<sup>30</sup> who identified an anxiety disorder in 11 (85%) and major depressive disorder in 5 (38%) of 13 children with functional RAP in specialty pediatric clinics, and with those of Liakopoulou-Kairis et al,<sup>35</sup> who identified a psychiatric disorder in 82% of RAP patients. Study results are also consistent with earlier findings that childhood RAP predicts anxiety, depression, hypochondriacal fears, and concerns about physical health in young adulthood.<sup>54,55</sup>

The most significant limitation of the current study is its cross-sectional nature, which precludes causal inference and limits our ability to draw conclusions beyond the recognition of significant associations. Although our finding that anxiety disorders precede the development of RAP in the majority of comorbid cases is interesting, the retrospective nature of the age of onset data limits our ability to draw firm conclusions. Study of the association between functional RAP and anxiety disorders nevertheless has the potential to inform future treatment and prevention efforts and to direct the search for mechanisms underlying the observed nonrandom associations.<sup>56</sup> Potential explanations for the strong observed association of RAP with anxiety disorders include unidirectional causal models (ie, one disorder causes the other) and shared diathesis models (ie, the disorders

share a common underlying risk factor or factors or are different aspects of a singular causal process), as well as study artifact.<sup>56</sup> Artifact alone is unlikely to provide an explanation for the strong association observed between RAP and anxiety in this study, particularly given our decision to drop somatic items from study psychiatric assessments and questionnaires and our efforts to minimize referral bias. Could anxiety “cause” RAP? Could anxiety or depression share a common diathesis with RAP or represent different aspects of the same disorder? Perhaps, but meaningful answers to such questions must await longitudinal studies, family/genetic studies, and psychobiological investigations.

This study is the first to systematically document higher levels of anxious temperament in children with RAP compared with pain-free control subjects. Because a single factor may confer vulnerability to a number of phenomenologically different disorders,<sup>57</sup> the relatively strong association of temperamental harm avoidance with pediatric RAP is of special interest. Harm avoidance and related personality traits such as neuroticism and negative affect have been associated with behavioral inhibition, pessimistic worry, fear of uncertainty, a tendency to respond to environmental challenge at lower thresholds and perhaps with greater intensity, vulnerability to anxiety and depressive disorders,<sup>52,53,57,58</sup> and functional gastrointestinal symptoms in adults.<sup>59</sup> Higher levels of negative affect have previously been shown to increase the vulnerability of children with functional RAP to respond to daily life stress with abdominal pain.<sup>60</sup> Behaviorally inhibited temperament has been linked to differences in stress reactivity,<sup>61</sup> a tendency to activate neural circuits involved in generating distress responses to potentially threatening or uncertain stimuli,<sup>62</sup> and the development of anxiety disorders<sup>63</sup> and somatic complaints<sup>64</sup> in childhood. Findings of heightened sensitivity to gut visceral sensations,<sup>65,66</sup> excessive muscle tenderness, and a

lowered pressure-pain threshold<sup>67,68</sup> in children and adolescents with RAP may prove to be the expression of a more generalized sensitivity to perceived novel or threatening stimuli.

Study results have important implications for the management of pediatric functional RAP. First and foremost, clinicians need to recognize that the vast majority of affected children will have an anxiety or a depressive disorder and that clinical management strategies and the design of clinical trials of intervention should take this reality into account. Treatments that are capable of addressing both the somatic and the emotional distress associated with RAP thus seem ideal. Two small randomized controlled trials of a cognitive behavioral psychotherapeutic intervention for RAP found that reductions in symptoms of emotional distress were associated with concomitant decreases in abdominal pain across treatment,<sup>69,70</sup> providing some support for the notion that treatments that are proved to be efficacious for pediatric anxiety or depressive disorders such as cognitive behavioral therapy<sup>71-73</sup> and some selective serotonin reuptake inhibitors<sup>74-77</sup> may be worthy of study as future treatments for functional RAP. The high observed rates of anxiety and depressive disorders in association with RAP also call into question the relatively common but poorly studied practice among gastroenterologists and some pediatricians of prescribing tricyclic antidepressants (TCAs) to children with functional RAP.<sup>29</sup> TCAs lack proven efficacy for pediatric anxiety and depressive disorders and are associated with problematic side effects, a low therapeutic index, and a small but real risk of sudden death in treated children.<sup>78</sup> Developing feasible and safe treatments for functional RAP that are capable of treating comorbid anxiety and depression in the medical setting could potentially minimize exposure of affected children to TCAs and other untested treatments, circumvent known problems with physician recognition of psychiatric disorder, and minimize the stigma associated with specialty mental health referral.

#### ACKNOWLEDGMENTS

Dr Campo was supported by National Institute of Mental Health Grant MH 01780 and in part by National Institute of Mental Health Grant MH 66371, Advanced Center for Interventions and Services Research for Early-Onset Mood and Anxiety Disorders (Dr Brent, principal investigator).

We are grateful for data collection by Michelle Saunders; the advice and encouragement of Drs Ron Dahl, Kelly Kelleher, David Kupfer, and James Perel; and the steadfast support and cooperation of Drs Harold Altman and David Wolfson and the physicians, staff, and administration of Children's Community Pediatrics, without whom this work would not have been possible.

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*Pediatrics* 2004;113;817-824  
DOI: 10.1542/peds.113.4.817

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