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Functional abdominal pain in childhood and adolescence increases risk for chronic pain in adulthood

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Abstract

A few studies of long-term outcomes for pediatric functional abdominal pain (FAP) have assessed acute non-abdominal pain at follow-up, but none has assessed chronic pain. We followed a cohort of pediatric patients with FAP ($n = 155$) and a well control group ($n = 45$) prospectively for up to 15 years. Participants ranged in age from 18 to 32 years at a follow-up telephone interview. FAP patients were classified as Resolved ($n = 101$) versus Unresolved ($n = 54$) at follow-up, based on whether they reported symptoms consistent with the adult Rome III criteria for a functional gastrointestinal disorder. Headache symptoms and reports of chronic non-abdominal pain also were assessed at follow-up. In the Unresolved group, 48.1% reported one or more sites of chronic non-abdominal pain at follow-up, compared to 24.7% in the Resolved group and 13.3% in the control group, $p < 0.01$. More than half (57.4%) of the Unresolved group endorsed symptoms consistent with International Headache Society criteria for headache, compared to 44.6% of the Resolved group and 31% of controls, $p < 0.05$. One-third of the Unresolved group reported both headache and one or more sites of chronic non-abdominal pain at follow-up, compared to 17.8% of the Resolved group and 4.4% of controls. Youth with FAP that persists into adulthood may be at increased risk for chronic pain and headache. Examination of central mechanisms that are common across chronic pain disorders may enhance understanding of this subgroup of FAP.

Keywords

Functional abdominal pain; Migraine; Headache; Tension-type headache; Chronic pain; Pediatric

1. Introduction

Abdominal pain is a common recurrent pain complaint of childhood [22]. Medical evaluations often fail to reveal a pathophysiological explanation for children's persistent abdominal pain. Instead, the pain typically is functional, associated with a functional gastrointestinal disorder (FGID) such as irritable bowel syndrome or functional dyspepsia [5,27,30]. A recent review paper reported that chronic or recurrent abdominal pain persisted in nearly a third of youth followed for several years [13]. In a few studies, youth with

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Conflict of interest

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persistent abdominal pain also reported other pain complaints, particularly headaches, at follow-up [3,10,19,14]. This observation is consistent with studies of adults that report high co-morbidity of FGIDs with chronic pain syndromes such as fibromyalgia, headache, and back pain [1,15,17,23,35].

It is possible that functional abdominal pain (FAP) in childhood and adolescence is an early sign of vulnerability to chronic pain that becomes manifest in non-abdominal pain locations in adulthood. Potential explanations for the overlap previously reported between FGIDs and chronic pain in adults include a shared dysfunction in the central nervous system [20], psychological influences [34], and contextual factors such as social reinforcement of pain behavior [18]. Thus, there are theoretical reasons to expect pediatric FAP to be associated with chronic pain in adulthood.

The possibility that youth with persistent FAP may be at risk for comorbid chronic pain in adulthood has received little empirical evaluation. The few outcome studies of FAP that evaluated non-abdominal pain at follow-up did not assess whether non-abdominal pain was chronic, were not prospective cohort studies that extended into adulthood, and did not report base rates of non-abdominal pain in a healthy comparison group of adults. Thus, existing empirical data do not adequately describe the nature of chronic pain that may develop in youth with persistent FAP, nor do the data tell us whether youth with FAP are more likely than their peers without FAP to develop chronic pain in adulthood.

The current study systematically assessed chronic pain in adulthood in a cohort of pediatric FAP patients and well controls followed prospectively for up to 15 years. At follow-up, we assessed participants' reports of symptoms associated with the Rome III criteria for abdominal pain-related FGIDs in adults [12], symptoms associated with the International Headache Society criteria for headaches [8], and the presence of chronic pain at multiple body locations. We hypothesized that pediatric patients with FAP that persisted into adulthood would have a significantly higher prevalence of comorbid chronic pain and headache as adults compared to patients in the Resolved FAP group and controls without a childhood history of FAP. Based on reports that women have higher rates of FGIDs and chronic pain syndromes [25,28], we also examined the data for gender differences.

2. Methods

2.1. Sample

Participants in the current study were drawn from an ongoing prospective study of chronic abdominal pain in children and adolescents. Participants in the FAP group were recruited from former patients who presented to the Vanderbilt Pediatric Gastroenterology Clinic for evaluation of chronic or recurrent abdominal pain when they were 8–16 years of age and enrolled in one of several studies conducted by Walker and colleagues between 1993 and 2004 [e.g., 5,31]. Eligibility criteria for these original studies were abdominal pain of at least 3 months duration, no chronic illness, and no organic disease diagnosis for abdominal pain from the referring physician. The current study excluded patients whose medical evaluation at Vanderbilt yielded evidence of inflammatory bowel disease ($n = 2$). Only participants who had reached adulthood (defined as at least 18 years of age) at the time of follow-up were eligible for the current study. Of the 191 eligible participants invited to participate in the study, 36 declined participation, leaving a FAP sample of 155.

The healthy control group for the current study was recruited from control samples in Walker and colleagues' prior studies [31–33]. Participants for those samples were recruited from community schools and had no chronic illness and no abdominal pain in the month preceding initial study participation. Two of these participants reported symptoms consistent

with a Rome III FGID at follow-up and were excluded from the control group. Of the 53 eligible adult control participants invited to complete the current follow-up study, eight declined, leaving a control sample of 45.

The current study was conducted on average ($\pm$ SD) 10.7 ± 3.56 and 7.2 ± 2.51 years after participation in the original study for FAP and Healthy samples, respectively. A significant age difference was observed at follow-up between FAP and Healthy groups, $t(198) = -6.09$, $p < 0.01$. Participants in the FAP sample were older ($M = 22.9$ years, $SD = 3.52$) than those in the healthy control group ($M = 19.6$ years, $SD = 1.66$). The FAP and Healthy groups did not differ in gender composition or race/ethnicity, which was primarily non-Hispanic Caucasian.

2.2. Procedure

The Vanderbilt University Institutional Review Board approved all procedures. After providing informed consent, participants responded to a telephone interview about their health.

2.3. Measures

2.3.1. Persistent Pain Questionnaire (PPQ) [7]—Presence and location of chronic pain were assessed using a modified version of the Persistent Pain Questionnaire [7]. The PPQ provides a structured assessment of the history and location of chronic pain based on the standard eight body locations described by the International Association for the Study of Pain. We excluded the abdominal pain location from the PPQ because abdominal pain was assessed in detail with the Rome III questionnaire described below. For each location, respondents indicated whether they had ever had pain in that location “daily or almost every day that continued for 3 months or longer”, the operational definition of chronic pain employed in this study and prior work [7]. For each location endorsed, respondents indicated whether the chronic pain was current (had occurred within the 3 months prior to the interview) or if the pain preceded that time (had occurred more than 3 months prior to the interview). For current pain in each location, respondents rated the usual intensity of the pain on a scale from 0 (none) to 100 (the most pain possible). To narrow the focus of the current study to clinically meaningful chronic pain (i.e., greater than mild intensity), participants were considered to have current chronic pain in a particular body location if they reported a moderate or greater pain intensity (operationalized as a rating of 30/100 or higher) for that location. The total number (ranging from 0 to 7) of current chronic pain locations rated 30 or higher also was computed. Participants were considered to have a history of chronic pain in a particular body location if they reported that the pain lasted 3 months or longer during a period more than 3 months prior to the interview.

2.3.2. Rome III diagnostic questionnaire for functional gastrointestinal disorders [12]—The Rome III questionnaire was developed by the Rome Foundation Board based on the Rome III criteria for functional gastrointestinal disorders (FGIDs). It was designed to identify individuals who endorse the Rome III symptom criteria associated with various FGIDs. This study administered only the 24 questionnaire items that assess symptom criteria for the three FGIDs associated with abdominal pain in adults: irritable bowel syndrome, functional dyspepsia, and functional abdominal pain syndrome. Participants reported how often they had experienced each symptom in the past 3 months. Participants’ responses were scored to determine whether they currently met symptom criteria for each of the FGIDs. Former FAP patients who at follow-up met symptom criteria for one or more FGIDs associated with abdominal pain were classified as “Unresolved” and those who did not meet symptom criteria for any FGID associated with abdominal pain were classified as “Resolved”.

2.3.3. Headache interview—A structured headache interview was created to assess symptom criteria for migraine without aura, episodic tension-type headache, and chronic tension-type headaches based on the current revision of the International Headache Society (IHS) classification system. This structured interview was modeled after the interview used in previously published work by the last author and others that was designed to facilitate headache diagnosis by trained non-physicians using the previous version of the IHS diagnostic criteria [4,8]. Respondents answer a series of standard questions followed by open-ended probes that elicit further information regarding the quality, duration, frequency, and other characteristics of each type of headache reported by the respondent. Respondents may describe up to two types of headache experienced currently or in the past. For this study, each participant received scores indicating the presence or absence of symptoms consistent with IHS criteria for the headache subtypes noted above.

2.4. Statistical analysis

All analyses used SPSS for Windows Version 17 statistical package (SPSS, Inc., Chicago, IL). Preliminary analyses used *t*-tests for group mean comparisons and χ^2 tests for categorical measures. Primary study hypotheses were tested with a series of χ^2 analyses or Fisher's Exact Tests comparing healthy controls, Unresolved FAP, and Resolved FAP. All probability values reported are two-tailed with a $p < 0.05$ criterion for significance.

3. Results

Participants in the FAP group were classified into one of two groups, according to the status of their GI symptoms at follow-up. Of 155 participants in the FAP group, at follow-up 54 (35%) reported symptoms consistent with the adult Rome III adult criteria for an abdominal pain-related FGID and were classified as "Unresolved". The remaining 101 participants in the FAP group were classified as "Resolved". Table 1 presents demographic characteristics of the control, Resolved, and Unresolved groups. All groups included more women than men; there were no significant differences in gender composition across the three groups.

We examined the prevalence of chronic non-abdominal pain at follow-up in each group. In the Unresolved FAP group, 48.1% of participants reported 1 or more sites of chronic non-abdominal pain compared to 24.7% in Resolved FAP and 13.3% in the control group, $\chi^2 (4, N = 200) = 16.01, p < 0.01$. The prevalence of 1 or more sites of chronic non-abdominal pain did not differ by gender.

Table 2 shows the specific body locations of chronic non-abdominal pain for Unresolved FAP, Resolved FAP, and controls. The groups differed significantly in prevalence of current chronic pain of the shoulder/arm/hand, $\chi^2 (2, N = 200) = 15.51, p < 0.01$, pelvis, $\chi^2 (2, N = 200) = 12.88, p < 0.01$, back, $\chi^2 (2, N = 199) = 8.57, p < 0.05$, and leg/foot/knee/ankle, $\chi^2 (2, N = 199) = 7.54, p < 0.05$. The Unresolved FAP group had the greatest percentage of participants endorsing current chronic pain in each of these areas. There were no significant differences in any current chronic pain location based on gender.

With respect to headache, over half (57.4%) of the Unresolved FAP group described symptoms consistent with IHS criteria for a headache diagnosis in the previous 3 months, compared to 44.6% of Resolved FAP and 31% of controls, $\chi^2 (2, N = 200) = 6.87, p < 0.05$. Overall, a higher percentage of women (51.6%) endorsed symptoms reflecting IHS headache criteria than men (34.2%), $p = 0.02$ (Fisher's Exact Test). Table 3 presents the prevalence of symptoms consistent with IHS headache subtypes for controls, Resolved FAP, and Unresolved FAP.

Table 4 summarizes the prevalence of comorbid headache and chronic non-abdominal pain in the Unresolved FAP, Resolved FAP, and control groups. One-third (33.3%) of participants in the Unresolved group reported both headache and one or more sites of chronic non-abdominal pain, compared to 17.8% of the Resolved group and 4.4% of controls.

3.1. History of chronic pain in Resolved FAP, Unresolved FAP, and control groups

We also assessed whether participants had a prior history of chronic non-abdominal pain that occurred more than 3 months preceding the follow-up but had resolved at the time of the follow-up. Two thirds (65.8%) of participants with Unresolved FAP reported 1 or more sites of chronic non-abdominal pain that occurred more than 3 months prior to follow-up compared to 50.0% of Resolved FAP and 33.3% of control groups, $\chi^2(4, N = 200) = 9.73, p < 0.01$. There were no gender differences in the history of chronic non-abdominal pain more than 3 months preceding the follow-up.

Prior history of chronic pain (more than 3 months *prior* to follow-up) is shown by pain location in Table 5. Prior history groups differed significantly in prior history of chronic pain of the head, $\chi^2(2, N = 198) = 11.07, p < 0.01$, shoulder/arm/hand, $\chi^2(2, N = 199) = 8.73, p < 0.05$, and pelvis, $\chi^2(2, N = 200) = 9.93, p < 0.01$. The Unresolved FAP group had the greatest percentage of participants endorsing prior history of chronic pain in these areas. A greater percentage of women reported a prior history of chronic head pain (24.6%) than men (11.8%), $p = 0.03$ (Fisher's Exact Test). Significantly more women also reported a history of pelvic pain (13.7%) compared to men (3.9%), $p = 0.03$ (Fisher's Exact Test). No other gender differences in history of chronic pain were shown.

4. Discussion

We followed a cohort of pediatric patients with FAP prospectively into adulthood and identified two distinct long-term outcomes. The majority of FAP patients had recovered when interviewed as adults – they did not report symptoms consistent with adult Rome III criteria for an abdominal pain-related FGID. This rate of recovery (65%) is similar to that reported for other samples of FAP patients in a recent review paper [13] but has the methodological rigor of a prospective design and application of the Rome III symptom criteria for FGIDs. Thus, the good news is that FAP resolves during childhood for a majority of children evaluated at tertiary care centers.

A sizeable subgroup (35%) of pediatric patients with FAP, however, continued to report symptoms consistent with the Rome III criteria for abdominal pain-related FGIDs as adults. The majority of this subgroup also reported symptoms consistent with current IHS criteria for migraine and/or tension-type headache. Moreover, the majority of FAP patients with FGIDs also reported one or more sites of chronic non-abdominal pain at follow-up. They were significantly more likely than recovered FAP patients and controls to report current chronic pain (defined as 3 months or more of daily or near daily pain) in the pelvis, back, shoulder, and upper and lower limbs. Thus, this subgroup of FAP patients appeared to mature into adults with FGIDs and comorbid chronic pain and headache.

Several potential mechanisms may link FAP to chronic pain in adulthood. First, FAP itself may contribute to the development of chronic pain. Behavioral consequences of FAP, such as activity limitation that leads to physical deconditioning, may put children with FAP at risk for subsequent development of musculoskeletal pain. Social factors, such as parent attention and concern about FAP, may increase children's vigilance and fear of pain, lowering their threshold and tolerance for all types of pain. Finally, stressful circumstances

resulting from FAP, such as falling behind in school, may have negative effects on their health.

It also is possible that FAP does not play a causal role in the development of other chronic pain conditions but rather, in some patients, represents a centrally mediated augmentation of pain and sensory processes [11,36] that can be manifest in both visceral and somatic pain conditions. Central sensitization, that is, elevated responsiveness to nociceptive stimuli resulting from increased excitability of neurons in the dorsal horn of the spinal cord [2], is thought to occur in visceral pain disorders in humans [24] and might explain the link between pediatric FAP and chronic pain in adulthood. Indeed, results of an experimental pain study with a subset of participants from the current study showed that hypoalgesia related to elevated resting blood pressure which is present in healthy females is absent in females with a history of FAP [6], suggesting potential dysfunction in overlapping systems modulating pain and blood pressure. Epidemiologic studies suggest that multi-site chronic pain is more common than single-site chronic pain among adults [9,26] and is associated with higher levels of disability than single-site chronic pain [16]. We may enhance our understanding of pain-predominant FGIDs by considering them in relation to central mechanisms common across chronic pain disorders [21].

This study had several limitations that suggest directions for future research. First, although our baseline research protocol included assessment of acute non-specific somatic symptoms with the Children's Somatization Inventory [29], we did not evaluate chronic daily pain at that time. Therefore, the temporal relation between FAP and other chronic pain is unclear and we cannot rule out the possibility that FAP patients had experienced chronic daily non-abdominal pain for 3 months or longer at the time of their baseline assessment. Second, although our follow-up assessment of pain was the most thorough to date in an outcome study of FAP, we did not evaluate symptoms of specific pain conditions such as temporomandibular joint syndrome, interstitial cystitis, and fibromyalgia that often are comorbid with FGIDs in adults [34]. Third, we assessed FGIDs and chronic pain at follow-up with interviews that relied solely on participant self-reports and may have been impacted by limitations of participant memory; daily diary methods may provide more accurate symptom assessment. Finally, without a medical evaluation, we cannot rule out the possibility that undetected disease contributed to pain reported at follow-up.

An obvious next step in this research is to identify characteristics of pediatric patients with FAP who are at risk for chronic pain and headache in adulthood. If these children can be identified and treated, it may be possible to improve their long-term outcomes. It will be important to assess the effect of treatment for FAP on both abdominal and non-abdominal pain. If the mechanisms of FAP differ for a subgroup at risk for other types of chronic pain, that subgroup may require different interventions than those designed for FAP in general.

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Table 1

Participant characteristics.

Variable	Participant type		
	Healthy	Resolved	Unresolved
<i>n</i>	45	101	54
Age (years)*	19.56 ± 1.66	22.86 ± 3.58	22.85 ± 3.43
Gender (% female)	64.4	55.4	72.2
Race and ethnicity (% Caucasian)	91.1	88.1	98.1

Note: All means are presented as mean ± SD. Unresolved/(Resolved) refers to participants with FAP in childhood who at follow-up did/(did not) report symptoms consistent with the adult Rome III criteria for an abdominal pain-related functional gastrointestinal disorder.

*
 $p < 0.05$.

Table 2

Prevalence (%) of chronic pain at follow-up for each group by anatomical location.

Chronic pain location	Participant type			
	Control (<i>n</i> = 45)	Resolved (<i>n</i> = 101)	Unresolved (<i>n</i> = 54)	<i>p</i> -Value
Head (%)	2.2	10.0	14.8	–
Neck (%)	2.2	2.0	9.6	–
Shoulder, arm, hand (%)	2.2	4.0	20.4	<0.01
Chest (%)	0.0	3.0	3.7	–
Pelvis (%)	0.0	3.0	14.8	<0.01
Back (%)	9.1	11.9	27.8	<0.05
Leg, foot, knee, ankle (%)	4.0	8.9	20.8	<0.05

Note: Unresolved/(Resolved) refers to participants with FAP in childhood who at follow-up did/(did not) report symptoms consistent with the adult Rome III criteria for an abdominal pain-related functional gastrointestinal disorder.

Table 3

Prevalence (%) of headache subtypes at follow-up based on participants' reports of symptoms consistent with IHS criteria.

Headache type	Participant Type		
	Control (<i>n</i> = 45)	Resolved (<i>n</i> = 101)	Unresolved (<i>n</i> = 54)
Tension-type (%)	6.8	5.9	7.5
Migraine (%)	18.2	28.7	35.8
Both tension-type and migraine (%)	4.5	10.0	13.2
No headache (%)	70.5	55.4	43.4

Note: Unresolved/(Resolved) refers to participants with FAP in childhood who at follow-up did/(did not) report symptoms consistent with the adult Rome III criteria for an abdominal pain-related functional gastrointestinal disorder.

Table 4

Summary of current comorbid chronic pain and headache prevalence according to participant health status at follow-up.

Chronic pain type		Participants		
Non-abdominal pain	Headache	% Control	% Resolved	% Unresolved
		<i>n</i> = 45	<i>n</i> = 101	<i>n</i> = 54
No	Yes	26.7	26.7	25.9
Yes	Yes	4.4	17.8	33.3
Yes	No	13.3	11.9	14.8
No	No	55.5	43.6	25.9

Note: Data represent current chronic non-abdominal pain and headache. Non-abdominal chronic pain refers to pain in one or more of the following regions endorsed as having a severity score of 30 or greater: neck, shoulder, arm, hand, chest, pelvis, back, leg, feet, knees, or ankles. Headache refers to symptoms consistent with IHS criteria for migraine and/or tension-type headache subtypes. Unresolved/(Resolved) refers to participants with FAP in childhood who at follow-up did/(did not) report symptoms consistent with the adult Rome III criteria for an abdominal pain-related functional gastrointestinal disorder.

Table 5

Prevalence (%) of prior history of chronic pain for each group by anatomical location.

Chronic pain location	Participant type at follow-up			p value
	Control (n = 45)	Resolved (n = 101)	Unresolved (n = 54)	
Head (%)	4.4	20.6	31.4	<0.01
Neck (%)	6.7	7.8	17.3	–
Shoulder, arm hand (%)	4.4	12.7	25	<0.05
Chest (%)	2.2	4.9	9.8	–
Pelvis (%)	0.0	9.7	19.2	<0.01
Back (%)	15.6	27.2	36.5	–
Leg, foot, knee, ankle (%)	13.3	17.6	23.5	–

Note: “Prior history” was defined as three or more consecutive months of daily pain that occurred more than 3 months preceding the interview but had resolved at the time of the follow-up interview. Unresolved/(Resolved) refers to participants with FAP in childhood who at follow-up did/(did not) report symptoms consistent with the adult Rome III criteria for an abdominal pain-related functional gastrointestinal disorder.