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Multiple Psychological Factors Predict Abdominal Pain Severity in Children with Irritable Bowel Syndrome

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Abstract

Background—Anxiety and depression are implicated as contributors to abdominal pain in pediatric irritable bowel syndrome (IBS) but is unclear if this pain is associated with other psychological factors. The study objective was to test if the impact of anxiety or depression on IBS symptom severity is mediated by somatization and/or pain catastrophizing.

Methods—We utilized baseline data from local pediatric IBS clinical studies. Through mediation analysis, we assessed whether somatization or pain catastrophizing mediated (either independently or combined) the separate relationships of anxiety or depression with IBS abdominal pain severity.

Key Results—We analyzed 261 participants. All psychological factors were positively correlated with one another and IBS abdominal pain severity. The association of anxiety with IBS

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Author Contribution

MALvT originated the study idea. JMH, MALvT, DIC, MMS, and RJS developed the concept; JMH, EWB, and YL designed the study; JMH performed the data analyses and compiled the results; YL supervised all data analyses; JMH and DIC wrote the paper; all others critically revised the manuscript, read, and approved the final manuscript.

Disclosures

There are no conflicts of interest to report.

abdominal pain was mediated by both somatization and pain catastrophizing in individual analyses (each mediated standardized coefficient [β] 0.11, CI 0.05 – 0.18) and in multiple analysis (mediated standardized β 0.18, CI 0.09 – 0.27). The association of depression with IBS abdominal pain was also mediated by somatization (mediated standardized β 0.08, CI 0.02 – 0.14) and pain catastrophizing (mediated standardized β 0.06, CI 0.01 – 0.11) in individual analyses and in multiple analysis (mediated standardized β 0.19, CI 0.04 – 0.19).

Conclusions & Inferences—Somatization and pain catastrophizing mediate the relationships between anxiety/depression and IBS abdominal pain severity. These findings suggest that somatization and pain catastrophizing may be better treatment targets than anxiety and depression. Clinicians should assess these psychological factors in pediatric IBS patients and refer for intervention to improve outcomes.

Keywords

psychological factors; anxiety; depression; somatization; pain catastrophizing; irritable bowel syndrome; pediatric; mediation analysis

Introduction

Irritable bowel syndrome (IBS) is characterized by chronic abdominal pain and changes in stool consistency and/or stooling frequency not attributable to specific anatomic or biochemical abnormality (1, 2). IBS affects about 9% of children worldwide (3). Over half of affected children have abdominal pain symptoms into adulthood, which is associated with a $30 billion annual economic burden in the United States (4–9).

Compared to healthy children, children with IBS demonstrate increased psychological distress, specifically anxiety and depression, though symptom severity does not typically reach the level of a clinical diagnosis of an anxiety or depressive disorder (10–21). Moderate elevations in distress also exist in children with organic chronic conditions, suggesting the elevated distress in IBS may be a reaction to chronic symptoms (22–24). Alternatively, the biopsychosocial model of IBS suggests anxiety and depression may be important contributing factors to IBS symptoms; some data support increased anxiety preceding an IBS diagnosis (25, 26). Further, anxiety and depression are associated with abdominal pain outcomes within the population of children with IBS (27, 28).

Though anxiety and depression are most often studied, other psychological factors should be considered relevant to IBS outcomes. van Tilburg and colleagues provided a framework for exploring multiple psychological factors potentially involved in the symptom experience (29). Somatization is defined as experiencing symptoms affecting multiple organ symptoms that cannot be explained medically (30). Pain catastrophizing is an irrational expectation of the worst and feeling helpless in response to an actual or anticipated painful event (31). In adults with IBS, the authors found somatization and pain catastrophizing each better explain the relationship between anxiety and IBS symptom severity (29). These results suggest somatization and pain catastrophizing as potential important targets for psychotherapy in adults with IBS.

Evidence exists suggesting this same relation may be true for children. Our research group has shown somatization is associated with abdominal pain symptoms in children with functional abdominal pain (32). In a sample of healthy children without a functional abdominal pain disorder, Lavigne and colleagues found somatization mediated the relation between anxiety/depression and abdominal pain (33). Further, van Tilburg and colleagues demonstrated changes in pain catastrophizing, rather than anxiety or depression, explained the effect of cognitive behavioral therapy treatment on pediatric IBS pain (34). However, no study to date has specifically tested if the effects of anxiety/depression on IBS abdominal pain is better explained by somatization and pain catastrophizing. Therefore, we examined whether somatization or pain catastrophizing, either individually or combined, mediates the association of anxiety/depression and IBS abdominal pain symptom severity in children with IBS. We hypothesized that somatization and pain catastrophizing would both mediate the association of anxiety/depression with IBS abdominal pain severity and thereby identify a stronger association compared to the original relationship excluding these maladaptive processes.

Materials and Methods

Participants

This study utilized previously collected clinical study data from children with IBS. The participants' data were collected from a total of four observational and interventional pediatric clinical trials conducted at Baylor College of Medicine and Texas Children's Hospital in Houston, TX (35–38). One parent signed informed consent and the child provided assent prior to initiation of each study. Only participant baseline data prior to any intervention were utilized. At baseline each participant completed psychological and demographic measures and a validated two-week abdominal pain/stooling diary, which captured abdominal pain frequency and intensity during three periods throughout the day (morning, afternoon, and evening).

Demographics and IBS Abdominal Pain

Caregivers provided the child participants' age, gender, and race/ethnicity at enrollment through a self-report questionnaire. The use of a 2-week validated abdominal pain/stooling diary defined our IBS cohort based on Rome III criteria and our previously published algorithm (39–43). The diary captured the number of pain episodes per day and intensity of the abdominal pain when it occurred (35). For this study, IBS abdominal pain was measured by multiplying the number of pain episodes over a two-week period by the mean pain intensity when a pain episode occurred as rated on a 10-point scale, which has been utilized as an outcome in other clinical studies in the field (44–50).

Psychological Instruments

Anxiety and Depression—Anxiety and depression were measured using the Behavior Assessment System for Children, which assesses behavioral and emotional problems in children and adolescents through parent proxy- and child self-report (51, 52). Only self-reported scores were used for this study. One of the four clinical studies used the original edition of the BASC instrument; the other three studies used the later version BASC-2 (51,

52). BASC scores were converted to BASC-2 scores as per the manual (52). All BASC-2 child-reported anxiety and depression scale T-scores were transformed into their respective Z-score based on each scales' distribution in our cohort. These Z-scores were utilized for mediation analyses.

Somatization—Our studies captured child somatization using the Children's Somatization Inventory (CSI) (53). Children indicated the extent to which they were bothered by 35 non-specific symptoms such as headaches and nausea using a 5-point Likert scale (ranging from "not at all" to "a whole lot"). All item responses were summed into a total score. Total scores were then transformed into a Z-score based on our sample's distribution for mediation analysis to standardize our results.

Pain Catastrophizing—Pain catastrophizing was captured by two separate instruments for the four pediatric IBS clinical studies. Two of the four clinical studies used the child self-report of the Pain Catastrophizing Scale (PCS-C) (54, 55). The PCS-C is a validated 11-item survey answered on a 5-point Likert scale ranging from 0 to 4 (56, 57). All items are summed for a total score. Subscales for this survey includes Rumination (cannot stop thinking about pain), Magnification (concern about the seriousness of the pain), and Helplessness (how overwhelming the pain is). A Z-score was assigned to the total score value based on this instrument's sample distribution.

The two other clinical studies used the Pain Response Inventory (PRI), a validated 60-item survey designed to assess coping skills for children with chronic pain using a 5-point Likert scale ranging from 0 to 4 (45, 58, 59). We used questions from the Catastrophizing and Distract/Ignore subscales, which were very similar to the PCS-C questions and reflected the Rumination, Magnification, and Helplessness dimensions described above. To calculate our PRI-derived catastrophizing total score variable, we summed the responses from the PRI Catastrophizing Scale and reverse coded 3 item responses from the PRI Distract/Ignore Scale (items 34, 44, and 48) (e.g., Try to think of something pleasant to take you mind off the pain). The 8 items were summed and Z-scores were calculated based on the sample distribution for this specific instrument (Supplementary Table C). Then the Z-scores from both the PCS-C and PRI were combined to create a single pain catastrophizing variable that was utilized for all analyses.

Statistical Analysis

Age, gender, and race/ethnicity were covariates for all analyses. We included only participants who had complete data for all variables and covariates of interest. A sensitivity analysis was conducted to compare excluded participants and the original cohort to assess for any biases in our cohort.

Bivariate correlation analysis evaluated the association between each of the psychological variables and IBS abdominal pain. Multiple linear regression modeling then assessed concurrently the association of the psychological variables with IBS abdominal pain. Statistical significance in multiple linear regression modeling for anxiety and depression predicting IBS abdominal pain severity was a required precondition for proceeding to mediation analyses to assess the whether these relationships are affected by somatization and

pain catastrophizing. Multicollinearity was also assessed via the variance inflation factor, indicating that multicollinearity was not problematic (i.e., variance inflation factor < 4 for all variables).

Mediation Analysis—Mediation can be described as the introduction of a third variable that explains the relationship of an established two-variable system (60). In other words, the association between two variables may be significant, but a third mediating variable accounts for the variance initially attributed to the original two variable relationship. Figure 1 represents a generic model for mediation analysis in this study. We examined whether the association between anxiety or depression (independent variables) and the dependent variable of IBS abdominal pain can be better explained alone (path *c*) or in the presence of a mediating variable(s) (paths *a* and *b*). When mediation occurs, the indirect relationship summarized in path c' is smaller than the direct relationship summarized in path *c* (Figure 1).

We first conducted individual mediation analysis by evaluating separately the impact of a single mediator (i.e., somatization or pain catastrophizing Z-scores) on the relationship between our independent variables (i.e., anxiety or depression Z-scores) and the dependent variable of IBS abdominal pain severity Z-scores. Each analysis calculated the standardized coefficient (β) and its 95% confidence interval (CI) for each direct and indirect relationship (paths *a*, *b*, *c*, and c'). If both mediators were significant in individual mediation analysis, we then conducted multiple mediation analysis to assess to what degree anxiety/depression and IBS abdominal pain were affected by dual mediators of somatization and pain catastrophizing in a multiple mediation model.

Statistical analyses were performed in SPSS Statistics 25 for Windows software (IBM Corporation, Armonk, NY). The average and standard deviation were calculated for age and proportions for the other demographic categorical variables. We computed the mean, standard deviation, range, and Z-score for all psychological variables and IBS abdominal pain. Statistical significance for all analyses was defined as $P < 0.05$. The mediation analysis was conducted in SPSS Statistics using PROCESS version 3.0 extension (61). Bootstrap estimation with 1,000 samples was used to test the indirect effects of the mediator(s) in the individual and multiple mediation tests. Significant mediation results were defined by a 95% confidence interval range that does not contain zero (61).

Results

Our initial cohort included 283 children with IBS who completed psychological instruments and a baseline 2-week abdominal pain/stooling diary (n=86 from an interventional clinical study and n=197 from non-interventional studies). Of this sample, 261 participants had completed data for all covariate and psychological variables. Sensitivity analysis between the original cohort and the 22 excluded participants revealed a small but clinically irrelevant difference in age (10.3 ± 2.5 vs 9.2 ± 1.6 years old, P=0.03) and no difference in regard to gender (P=0.14) or race/ethnicity (P=0.36) proportions (data not shown). Demographic characteristics of the IBS cohort are summarized in Table 1. Our cohort was mostly female (65.1%) (Table 1A). A range of races/ethnicities were represented.

Descriptives of psychological variables and the IBS abdominal pain severity composite score are outlined in Table 1B. All variables showed wide variation, which was ideal for our planned mediation analyses (Table 1B). The bivariate correlation analysis of all psychological variables and the IBS abdominal pain severity composite Z-scores revealed significant positive correlations for all (Supplemental Table A).

Hierarchical multiple linear regression then examined how these psychological variables were associated with IBS abdominal pain using age, gender, and race/ethnicity as covariates. Model 0 demonstrated the effect of the covariates on IBS abdominal pain severity, with gender ($P < 0.001$) being the only significant variable in this model (Supplementary Table B). Model 1 and Model 3 illustrate that anxiety ($P = 0.02$) and depression ($P < 0.001$) were each significantly associated with IBS abdominal pain severity after adjustment for the covariates, respectively (Supplementary Table B), and these results met the required precondition to proceed with mediation analysis for both anxiety and depression and the dependent outcome of IBS abdominal pain severity. The addition of somatization and pain catastrophizing in Model 2 rendered anxiety no longer significant (Supplementary Table B). The addition of somatization and pain catastrophizing with depression did not change its statistical significance status in Model 4 (Supplementary Table B).

Meditation Analyses

We next assessed whether somatization or pain catastrophizing individually mediated the relationship between anxiety or depression and IBS abdominal pain severity (Table 2). Results revealed that both somatization (mediated standardized β 0.11) and pain catastrophizing (mediated standardized β 0.11) were each significant mediators of the relationship between anxiety and IBS abdominal pain severity (Table 2). Individual mediation analysis also revealed that both somatization (mediated standardized β 0.08) and pain catastrophizing (mediated standardized β 0.06) were significant mediators of the association between depression and IBS abdominal pain severity (Table 2).

Multiple mediation analysis including both somatization and pain catastrophizing as mediators in the relationship between anxiety and IBS abdominal pain severity reinforced the findings of the previous individual mediation analyses (Figure 2). This multiple mediation model with anxiety predicting IBS abdominal pain severity indeed was mediated by both mediators and had a completely standardized mediated effect of 0.18 (95% CI 0.09 – 0.27). The mediated effect of somatization was a standardized effect of 0.09 or 51% of the total mediated effect, and the mediated effect of pain catastrophizing was 0.09 or 49% of the total mediated effect.

Similarly, somatization and pain catastrophizing were dual mediators of the association between depression and IBS abdominal pain severity (completely standardized mediated effect of 0.11; 95% CI 0.04 – 0.19). The mediated effect of somatization was a standardized mediated effect of 0.06 or explains 59% of the total mediated effect. As expected, pain catastrophizing accounts for the remaining standardized mediated effect of 0.05 or 41% of the total mediated effect (Figure 3).

Discussion

Our study found that somatization and pain catastrophizing mediate the association between anxiety/depression and IBS abdominal pain severity in children. To our knowledge, this is the first study to examine associations of such a diverse set of psychological variables with abdominal pain severity in a well-characterized pediatric IBS patient sample. The findings may mean that the effects of anxiety and depression on IBS outcomes are indirect and through changes in somatization and pain catastrophizing. These results inform the structure of a comprehensive model explaining how multiple psychosocial measures impact symptomatology in children with IBS.

As all these psychological factors are amenable to treatment such as CBT, our findings suggest that focusing on reducing somatization and pain catastrophizing may have more direct effects on pain than reducing anxiety or depression. In fact, CBT treatment outcomes in both in adults and pediatric patients have been shown not to be explained through changes in anxiety but rather changes in pain catastrophizing (34, 62).

Our findings are in agreement with previous work by van Tilburg and colleagues in adults who found that somatization and pain catastrophizing mediate the association between anxiety and abdominal pain symptoms (29). Furthermore, a community based study in a non-clinical sample of children and adolescents, found that somatization mediated the relationships of anxiety/depression and abdominal pain (33). Williams and colleagues also reported that somatization is more strongly associated with pain severity than anxiety, although they did not test for mediation (32). Other studies suggest that these maladaptive thought processes may also effect other health outcomes in children with abdominal pain. For example, pain catastrophizing is positively associated with functional disability and maintenance of pain (63, 64). Somatization has been associated with increased medical health visits as well as pain maintenance into adulthood (65, 66). These findings support the notion that pain catastrophizing and somatization may need to be considered in the diagnoses, treatment, and management of children with IBS.

Although we have evidence that pain catastrophizing can be changed with CBT, there is limited evidence of how to reduce somatization in either children or adults with IBS. Given the importance of both pain catastrophizing and somatization, there is a clear need to develop better efficacious treatments to reduce these maladaptive factors in affected children.

Limitations of this study includes the inability to determine causation based on the cross sectional nature of our data. The study outcome is a composite value of abdominal pain frequency and intensity thus we are not able to determine which pain characteristic is the key determinate of our observed results. However, there is lack of consensus whether abdominal pain frequency or intensity should be the primary pain outcome for IBS clinical trials (67, 68). In addition, the pain catastrophizing variable utilized was based on two separate methodologies and a universal score based on the respective instrument's Z score. Nonetheless, the two instruments utilized were derived from validated instruments with similar questions and they both capture similar related information. The strength of this

study is the ability to analyze multiple pertinent psychological measurements concurrently in a large group of children with IBS. In addition, we utilized a well-characterized IBS cohort.

In conclusion, our study illustrates the importance of evaluating and treating somatization and pain catastrophizing to improve abdominal pain symptomatology in children with IBS. More research is needed to determine how to best address these psychological factors in affected children to optimize psychological treatment efficacy and minimize IBS abdominal pain severity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

IBS	irritable bowel syndrome
BASC	Behavior Assessment System for Children
BASC-2	Behavior Assessment System for Children, 2nd edition
CSI	Child Somatization Inventory
PCS-C	pain catastrophizing scale-child self-report
PRI	Pain Response Inventory

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Key Points

- Anxiety, depression, somatization, and pain catastrophizing are associated with abdominal pain in children with irritable bowel syndrome (IBS). The interrelationships among these psychological conditions are unclear. Understanding how these factors are related may be important for the development of psychological treatments.
- We discovered that both somatization and pain catastrophizing, individually and combined, mediate the individual associations between anxiety/depression and IBS abdominal pain.
- Identifying and clinically treating somatization and pain catastrophizing in children with IBS may improve abdominal pain outcomes.

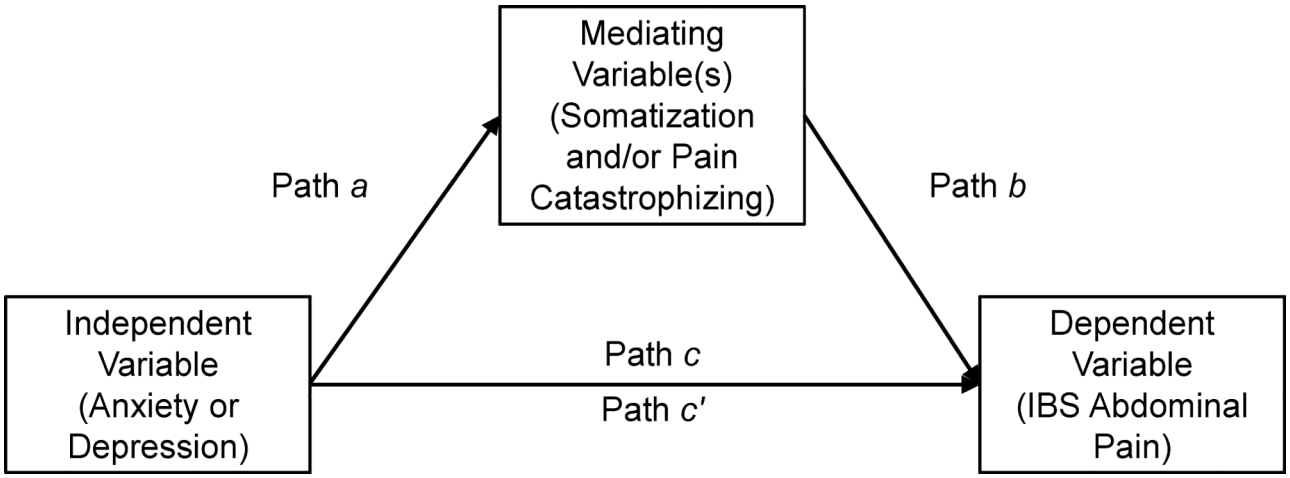

Figure 1. Conceptual Model of Mediation Analysis for Psychological Factors on IBS Abdominal Pain

Path *a* represents the effect of the independent variable on the mediator(s).

Path *b* represents the effect of the mediator(s) on the dependent variable.

Path *c* illustrates the total effect which considers both the relationship of the independent variable on the dependent variable and other indirect or mediating effects.

Path c' captures the direct effect of the independent variable on the dependent variable in the presence of other mediator(s).

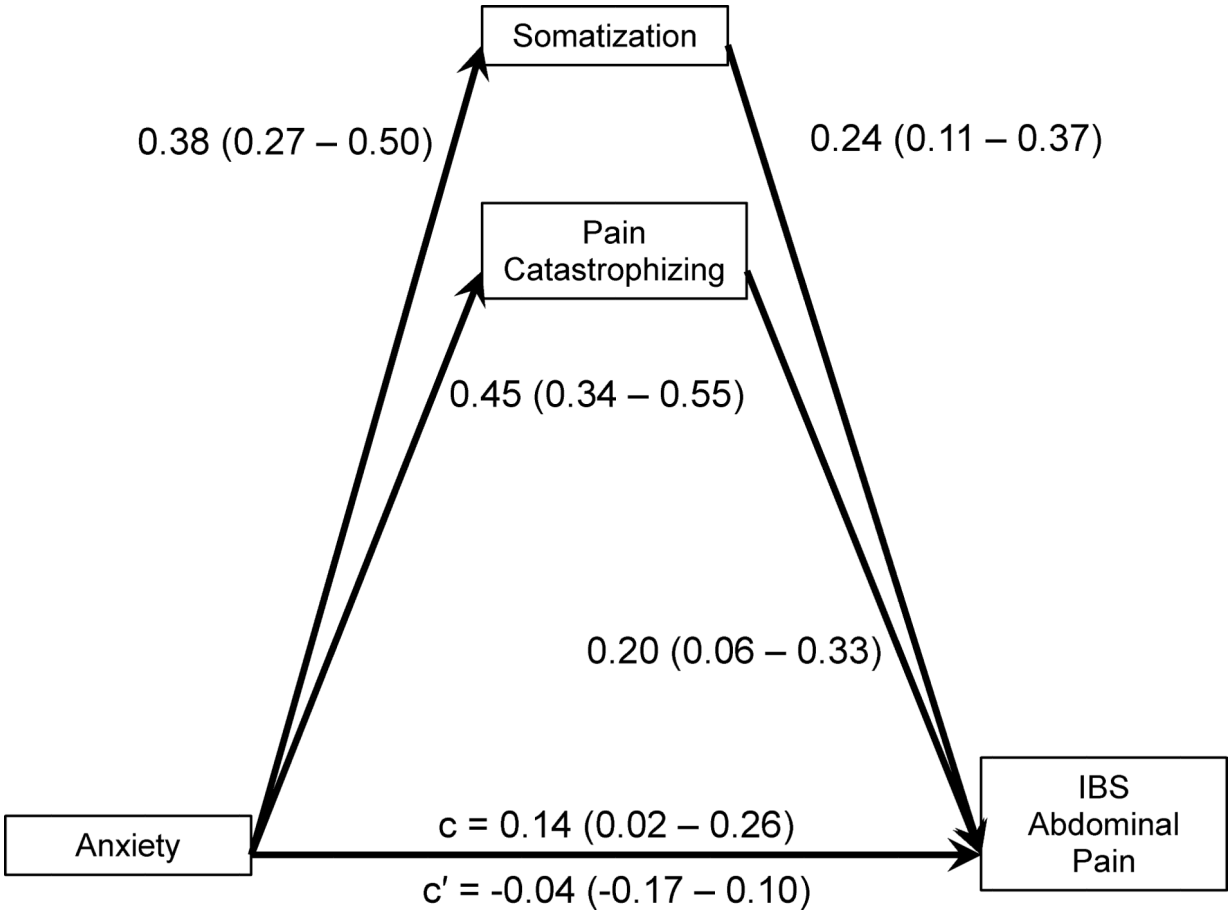

Figure 2. Mediation of Anxiety and Multiple Psychological Mediators on IBS Abdominal Pain by Somatization and Pain Catastrophizing

Denotes standardized coefficients (bootstrapping 95% confidence interval) between psychological factors and/or dependent variable. Statistical significance is defined as the confidence interval not containing 0.

Model is adjusted by the covariates of age, gender, and race/ethnicity.

The indirect effect of the mediators somatization and pain catastrophizing present: 0.18 (95% CI 0.09 – 0.28).

IBS, irritable bowel syndrome

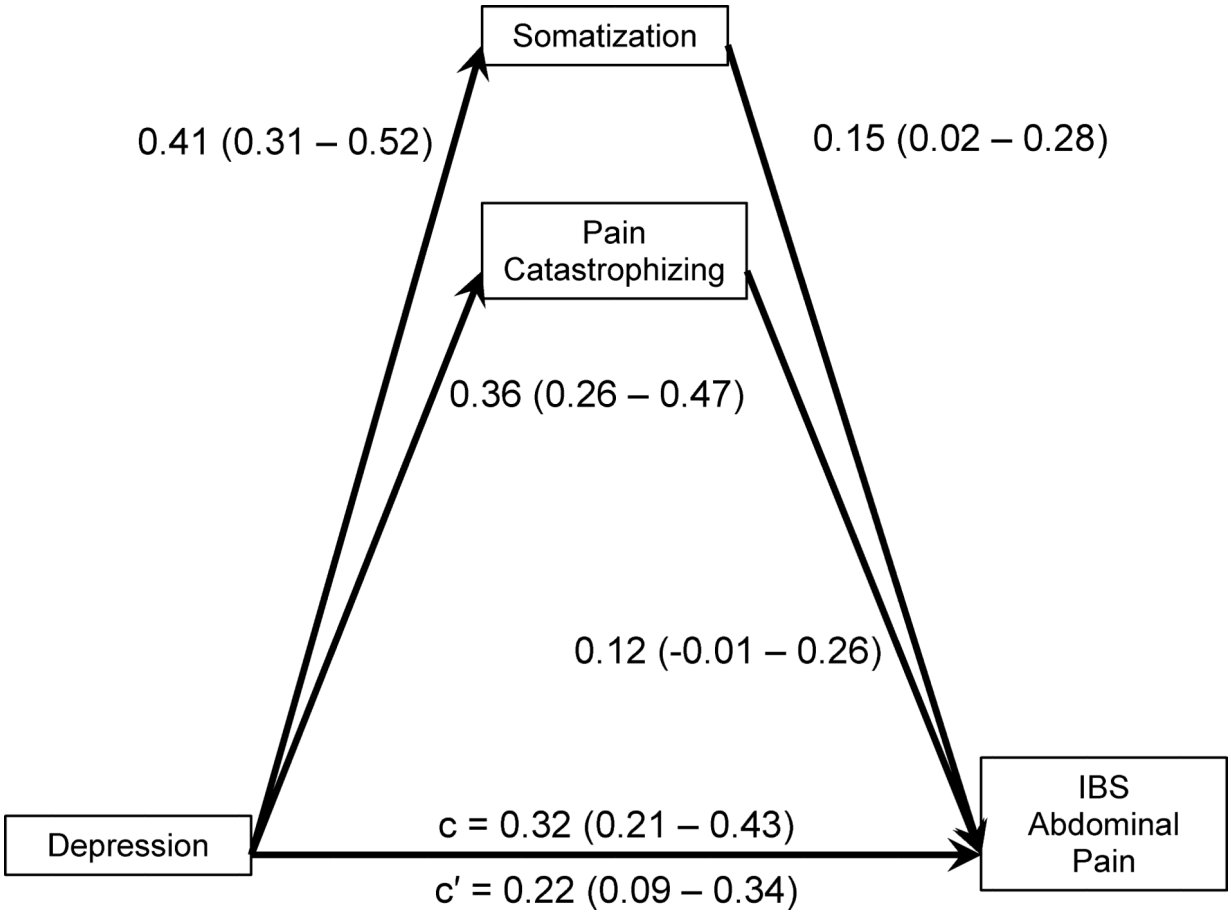

Figure 3. Mediation of Depression and Multiple Psychological Mediators on IBS Abdominal Pain by Somatization and Pain Catastrophizing

Denotes standardized coefficients (bootstrapping 95% confidence interval) between psychological factors and/or dependent variable. Statistical significance is defined as the confidence interval not containing 0.

Model is adjusted by the covariates of age, gender, and race/ethnicity.

The indirect effect of the mediators somatization and pain catastrophizing present in the model: 0.11 (95% CI 0.04 – 0.18).

IBS, irritable bowel syndrome

Table 1.

Child Participant Demographics and Psychological and Abdominal Pain Characteristics

A. Demographics		
Demographics	**Total Cohort (n=261)**	
Age, mean (SD) (years old)	10.4 (2.6)	
Gender Female, n (%)	170 (65.1)	
Race/Ethnicity, n (%)		
White, Non-Hispanic	155 (59.4)	
Black, Non-Hispanic	36 (13.8)	
Hispanic	57 (21.8)	
Others	13 (5.0)	
B. Psychological and Abdominal Pain Characteristics		
Psychological and Abdominal Pain Factors	**Mean (SD) Range**	**Z-Score Range**
BASC-2 Child Self-Report Anxiety Scale T-Score*	51.5 (11.0) (34 – 80)	−1.60 – 2.60
BASC-2 Child Self-Report Depression Scale T-Score*	47.8 (8.6) (40 – 86)	−0.91 – 4.45
Child Self-Report Somatization Inventory Total Score	28.5 (18.4) (0 – 104)	−1.54 – 4.10
Pain Catastrophizing Z-scores**	0.12 (0.9) (−2.38 – 2.5)	−2.38 – 2.50
IBS Abdominal Pain Intensity and Frequency Composite Score	48.0 (43.3) (2 – 224)	−1.06 – 4.06

*Some participants BASC scale T scores were converted to BASC-2 scale T scores

**This is based on either the 11-item Child Self-Reported Pain Catastrophizing Scale Z-scores or 8-item select questions from the Pain Response Inventory summed score Z-scores

BASC, Behavioral Assessment System for Children; BASC-2, Behavioral Assessment System for Children, 2nd Edition; IBS, irritable bowel syndrome

Table 2.

Individual Mediation Analyses of Psychological Factors on IBS Abdominal Pain

Independent Variable	Mediator	Path a β (CI)	Path b β (CI)	Path c β (CI)	Path c′ β (CI)	Mediated β (CI)
Anxiety	Somatization	0.38 (0.27 – 0.50)	0.28 (0.15 – 0.41)	0.14 (0.02 – 0.26)	0.03 (−0.09 – 0.16)	0.11 (0.05 – 0.18)
Anxiety	Pain Catastrophizing	0.45 (0.34 – 0.55)	0.25 (0.11 – 0.39)	0.14 (0.02 – 0.26)	0.03 (−0.10 – 0.16)	0.11 (0.05 – 0.18)
Depression	Somatization	0.41 (0.31 – 0.52)	0.18 (0.05 – 0.31)	0.32 (0.21 – 0.43)	0.25 (0.12 – 0.37)	0.08 (0.02 – 0.14)
Depression	Pain Catastrophizing	0.36 (0.26 – 0.47)	0.16 (0.03 – 0.28)	0.32 (0.21 – 0.43)	0.27 (0.14 – 0.39)	0.06 (0.01 – 0.11)

β is the standardized coefficient of the specific interaction as outlined in the paths in Figure 1.

The CI in each path noted are the bootstrapping CIs with 95% confidence. Inclusion of 0 within the CI indicates statistical non-significance.

Model controlled for the covariates of age, gender, and race/ethnicity

CI, confidence interval; IBS, irritable bowel syndrome