Behavioral Functioning in Youth With Inflammatory Bowel Disease: Perceived Barriers as Mediator of Medication Adherence

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Objectives   To examine the relationship between behavioral functioning specific to levels of attention and conduct problems and prescription medication adherence in youth with inflammatory bowel disease (IBD), and examine the mediational role of perceived barriers to adherence. Identifying potentially malleable factors associated with poor adherence such as behavioral functioning and barriers may guide treatment.   **Methods**   85 adolescents with IBD and their parents completed measures of adherence, attention and conduct problems, and barriers. To examine mediation models, indirect effects were tested using bootstrapping procedures outlined by Preacher & Hayes (2004, 2008).   **Results**   The majority of participants reported normative levels of attention and conduct problems. Higher levels of attention problems, conduct problems, and barriers were negatively associated with adherence. Bootstrapping procedures indicated that barriers mediated the effects of behavioral functioning on adherence.   **Conclusions**   Barriers may be a proximal factor contributing to the relationship between everyday behavioral functioning and adherence in youth with IBD.

Key words   adherence; attention; barriers; behavioral functioning; conduct; inflammatory bowel disease.

Crohn's disease and ulcerative colitis, jointly referred to as inflammatory bowel disease (IBD), are chronic immune-mediated diseases of the digestive tract that are often diagnosed in adolescence (Sandler & Eisen, 2000) and affect approximately 71 of 100,000 youth aged <20 years in the United States (Kappelman et al., 2007). Oral medications, including anti-inflammatories, immuno-modulators, corticosteroids, and antibiotics, are fundamental for successful treatment of IBD. Medication adherence is a significant concern for youth with IBD, particularly for adolescents, who are among the least adherent of age groups (DiMatteo, 2004).

Past research assessing adherence in youth with IBD has produced rates ranging from 12 to 98% depending on the sample, class of medication, and assessment methodology (Hommel, Davis, & Baldassano, 2009; Mackner & Crandall, 2005; Reed-Knight, Lewis, & Blount, 2011). Mackner and Crandall (2005) found

only 48% of adolescents and 38% of parents reported the adolescent as ''always adherent'' to IBD medications. Recent research has documented the occurrence of both accidental and volitional nonadherence in youth with IBD, with higher rates of volitional nonadherence related to greater disease activity and poorer parent-reported psychosocial quality of life (Schurman, Cushing, Carpenter, & Christenson, 2010). Consequences of nonadherence can include lower quality of life, additional and otherwise unnecessary prescriptions, drug interactions, drug resistance, and increased disease symptoms and severity (Hommel, Denson, & Baldassano, 2011; Kane, Huo, Aikens, & Hanauer, 2003; Quittner, Modi, Lemanek, Levers-Landis, & Rapoff, 2008). Given low documented adherence for youth with IBD and the potential negative outcomes, additional research is needed to examine potentially modifiable factors associated with poor adherence.

Using a risk and protective factors conceptual framework (Blount, Bunke, & Zaff, 2000), factors associated with adherence can be considered either fixed or malleable and potentially changeable through effective intervention. Several studies have documented a relationship between potentially malleable emotional and behavioral factors in youth with chronic illnesses and poorer adherence. For example, low treatment adherence has been found to be associated with higher self-reported anxiety and depression (Brownbridge & Fielding, 1994) and the presence of a psychiatric diagnosis (e.g., major depression, oppositional defiant disorder, and adjustment disorders; Shaw, Palmer, Blasey, & Sarwal, 2003). In a particularly applicable study to the current one, Gerson, Furth, Neu, and Fivush (2004) examined adherence and modifiable psychosocial variables in transplant recipients and found adherence to be positively related to better general child behavior and negatively related to parent-reported attention problems.

In youth with IBD, research has primarily focused on documenting rates of internalizing disorders and emotional functioning (Mackner, Sisson, & Crandall, 2004), with less focus on symptoms of externalizing disorders or general behavioral functioning (Hommel, Denson, Crandall, & Mackner, 2008). A recent study in youth with IBD demonstrated that externalizing behavior problems accounted for the majority of the variance in family functioning, suggesting that behavioral functioning may have greater impact on youth with IBD than previously thought (Odell, Sander, Denson, Baldassano, & Hommel, 2011).

Perceived barriers to medication adherence, which are specific behaviors or attitudes that occur close in time to medication taking such as forgetting, refusal/defiance, poor organization, regimen complexity, and side effects, are one potential mechanism by which a child's everyday behavioral functioning might be related to medication adherence. Differences in behavioral functioning may impact the barriers that adolescents and their parents perceive as getting in the way of taking prescribed medication. Primarily guided by the Health Belief Model (Bush & Iannotti, 1990), barriers have consistently been found to be associated with poorer adherence (Bond, Aiken, & Somerville, 1992; Simons & Blount, 2007; Simons, McCormick, Devine, & Blount, 2010; Zelikovsky, Schast, Palmer, & Meyers, 2008). Modi and Quittner (2006) examined barriers to treatment adherence in youth with cystic fibrosis and asthma and identified oppositional behaviors specific to the medical regimen as some of the most frequently reported barriers by children and parents to pulmonary adherence tasks.

In adolescents with IBD and their caregivers, Ingerski, Baldassano, Denson, & Hommel (2010) found that the most commonly endorsed barriers were forgetting, being away from home, interference with an activity, refusal/defiance, ran out/did not fill the prescription, not feeling well, and belief that medication is not necessary. Similarly to Modi and Quittner (2006), this study identified refusal/defiance as a frequently endorsed barrier, although neither study was designed to identify individual differences in general behavioral disorders that might also be related to adherence and the presence of the reported defiance related to adherence. Greenley, Stephens, Doughty, Raboin, & Kugathasan (2010) also examined barriers to adherence in youth with IBD and found that more barriers were related to imperfect adherence. Recently, youth with IBD experiencing both higher barriers and anxiety/depressive symptoms reported significantly lower medication adherence, highlighting the importance of considering proximal factors such as barriers as well as distal factors such as emotional and behavioral functioning (Gray, Denson, Baldassano, & Hommel, 2012).

In sum, pediatric research indicates that perceived barriers, including refusal specific to adherence, are associated with poorer medication adherence (Ingerski et al., 2010; Modi & Quittner, 2006). In addition, research has found that potentially modifiable emotional and behavioral factors, including attention, are associated with poorer adherence (Gerson et al., 2004; Shaw et al., 2003). First, the current study sought to advance the literature by examining the relationship between behavioral functioning (i.e., symptoms of attention problems and conduct problems measured on a continuous scale), perceived barriers, and prescription medication adherence in youth with IBD. The target sample was youth with IBD presenting for outpatient gastrointestinal care as opposed to a clinical sample of youth with diagnosed attention and conduct problems so that results would be most applicable to the majority of youth with IBD. Second, the current study sought to examine the potential mediational role of perceived barriers in the hypothesized relationship between behavioral functioning and medication adherence. We hypothesized the following: (a) parent report of symptoms of attention and conduct problems would be negatively related to both parent and adolescent report of prescription medication adherence; (b) parent and adolescent report of barriers to medication adherence would be negatively related to parent and adolescent report of prescription medication adherence; (c) parent report of symptoms of attention and conduct problems would be positively related to both parent and adolescent report of barriers to medication adherence; and (d) barriers to medication adherence would mediate the relationship between levels of attention and conduct problems and prescription medication adherence.

Although there are limitations to using only parent report of behavioral functioning, research has supported the validity of parent-reported behavioral problems by demonstrating better parent–adolescent agreement for externalizing behaviors compared with internalizing behaviors (Rey, Schrader, & Morris-Yates, 1992).

Method
Participants

Participants were 85 adolescents aged 11–18 years ($M = 14.76$, $SD = 2.27$) with a diagnosis of IBD and a primary caregiver. Parent respondents self-identified as the adolescent's mother (80%), father (19%), or grandmother (1%). Participants for this study were part of a larger study examining adherence in youth with IBD. Demographic characteristics of the sample can be seen in Table I. Participants were recruited from a large pediatric gastroenterology practice in the southeast United States. Inclusion criteria were: (a) diagnosis of Crohn's disease, ulcerative colitis, or indeterminate colitis; (b) 11–18 years of age, (c) prescribed oral medications for the treatment of IBD; and (d) English fluency. Exclusion criterion was parent-reported or chart-recorded developmental delay. No participants were excluded for this reason. Eight parent–child dyads were not included in the current analyses owing to incomplete data. During enrollment, 109 parent–adolescent dyads were consecutively approached for participation, with 93 consenting, for an 85% participation rate. Reasons for declining included lack of time ($n = 5$), lack of interest ($n = 6$), adolescent feeling too ill ($n = 3$), and adolescent choosing not to indicate ($n = 2$).

Measures

A brief demographics questionnaire assessed the participant's age, gender, ethnicity, family income, diagnosis (Crohn's disease, ulcerative colitis, or indeterminate colitis), date of diagnosis, and parental highest education levels. Medical chart reviews were conducted to obtain disease activity ratings and currently prescribed medications, including the name, dosage frequency and amount, and purpose of each medication.

Pediatric Crohn's Disease Activity Index
The Pediatric Crohn's Disease Activity Index (Hyams et al., 1991) is a measure of disease severity in pediatric Crohn's disease. The measure is scored from 0 to 100 based on (a) subjective reports (i.e., abdominal pain), (b) objective reports (i.e., fever), (c) laboratory findings, and (d) growth. Summed total scores provide indices of disease severity: inactive disease (≤ 10), mild to moderate disease (11–30), and severe disease (>30).

Table I. Demographic and Disease Characteristics of the Sample

Variable	N (%)
Child's sex (% female)	38 (45)
Child's IBD diagnosis	
Crohn's disease	64 (75)
Ulcerative colitis	21 (25)
PCDAI score ($n = 64$)	
Inactive disease (≤ 10)	34 (53)
Mild disease (11–30)	25 (39)
Moderate/severe disease (>30)	5 (8)
PUCAI score ($n = 21$)	
Inactive disease (<10)	9 (43)
Mild disease (10–34)	9 (43)
Moderate/severe disease (>34)	3 (14)
Race	
White	67 (79)
African American	10 (12)
Asian	1 (1)
Hispanic	4 (5)
Other	3 (3)
Median annual family income range	$75,000–$99,999
Maternal education level	
Some high school	1 (1)
High school diploma/GED	14 (16)
Some college	17 (20)
College degree	33 (39)
Professional degree	20 (24)
Paternal education level	
Some high school	2 (2)
High school diploma/GED	15 (18)
Some college	13 (15)
College degree	36 (43)
Professional degree	18 (21)
Missing	1 (1)

Note. IBD = inflammatory bowel disease; PCDAI = Pediatric Crohn's Disease Activity Index; PUCAI = Pediatric Ulcerative Colitis Activity Index.

Pediatric Ulcerative Colitis Activity Index
The Pediatric Ulcerative Colitis Activity Index (Turner et al., 2007) is a measure of disease severity for pediatric patients diagnosed with ulcerative colitis, which has been well validated against objective measures of disease status (Turner et al., 2010). Summed total scores from 0 to 85 provide indices of disease severity: inactive disease (<10), mild disease (10–34), moderate disease (35–64), and severe disease (≥ 65).

Medical Adherence Measure
The Medication Module of the Medical Adherence Measure (MAM; Zelikovsky & Schast, 2008) is a semi-structured interview to assess medication adherence to prescribed medications over the past 7 days. The MAM was

administered separately to parents and adolescents. To quantify adherence, the number of prescribed doses minus missed doses is divided by the number of prescribed doses, and multiplied by 100. Adherence for each prescription medication was assessed separately and then averaged across medications. Participants reported on the number of missed doses over the past 7 days to current prescription medications. Medications taken on an as-needed or p.r.n. basis were not considered in calculations of adherence. With renal transplant recipients, percentage of missed doses identified on the MAM was associated with the number of documented acute rejection episodes by 2 years after transplant ($r = .62$, $p < .001$) and significantly related to adherence as measured by the MEMS electronic technology, indicating the predictive and concurrent validity of the MAM with other measures of adherence (Zelikovsky et al., 2008).

Parent Medication Barriers Scale and Adolescent Medication Barriers Scale

The Parent Medication Barriers Scale (PMBS; Simons & Blount, 2007) is a 16-item measure that assesses parent-reported barriers to adolescents' medication taking. Respondents rate on a five-point Likert-like scale from "Strongly Disagree" to "Strongly Agree" how much they perceive each item to be a barrier to medication taking. A total score is calculated by summing items endorsed. The PMBS includes four barrier subscales: Disease Frustration/Adolescent Issues, Ingestion Issues, Regimen Adaptation/Cognitive Issues, and need for a Parent Reminder. The PMBS demonstrated adequate internal consistency, with a Cronbach's α of .83 for the total scale and α = .69 for Disease Frustration/Adolescent Issues, α = .66 for Ingestion Issues, and α = .77 for Regimen Adaptation/Cognitive Issues.

The Adolescent Medication Barriers Scale is the corresponding 17-item measure that assesses adolescent-reported barriers to taking medications. The Adolescent Medication Barriers Scale total score was used in the current study and demonstrated adequate internal consistency, with a Cronbach's α of .86.

Behavior Assessment System for Children—Second Edition (BASC-2), Parent Form

The BASC-2 is a behavior assessment questionnaire (Reynolds & Kamphaus, 2004). Parents rate how frequently behaviors occur from "Never" to "Almost Always." T-scores are used to compare respondents' answers with norms for same-gender and same-aged children. For the current study, age-appropriate versions of the two externalizing clinical scales measuring Attention

Problems and Conduct Problems were used. T-Scores between 41 and 59 fall in the average range, with successive 10-point increments representing "at risk" and "clinically significant" ranges. Scales demonstrated adequate internal consistency, with all Cronbach's α values >.70.

Procedure

Procedures were in accordance with Institutional Review Board approval. Consecutive recruitment occurred at a large outpatient pediatric gastroenterology clinic. Enrollees completed informed written consent and assent. Those who declined were asked to complete an anonymous demographics screener to compare participants with nonparticipants. Adolescent and parent participants independently self-reported on all measures, except the MAM, which was administered as a semi-structured interview separately to adolescents and their parents by the first author or trained assistants. Before completion of the MAM, charts were reviewed to obtain the current medication regimen. Interviews occurred in an examination room immediately before or after the medical appointment. Both parent and child participants were compensated for their time with a $20 gift certificate to a local retail store.

Data Analysis

The relationships between levels of adolescents' attention and conduct problems, barriers to adherence, and medication adherence were analyzed using two-tailed Pearson product correlation coefficients.

To examine the proposed mediation analyses, approaches that are best supported by the current literature were used. Specifically, the indirect effects of the models were tested using SPSS macros for single and multiple mediator models described by Preacher and Hayes (2004, 2008) and Hayes and Preacher (2012) and available at http://www.afhayes.com/spss-sas-and-mplus-macros-and-code.html. The indirect effect of the model was examined owing to shortcomings of the traditional Baron and Kenny (1986) criteria, including susceptibility to type I error, and low statistical power, especially in small sample sizes (MacKinnon, Lockwood, Hoffman, West, & Sheets, 2002; Preacher & Hayes, 2004). The indirect effect of the model is formally tested by producing a bootstrapped estimation of the indirect effect based on 5,000 iterations and a 95% confidence interval for this estimate. In the event that zero does not lie within the 95% confidence interval for the bootstrapped results for indirect effects, we can conclude that the indirect effect is significantly different from zero and that mediation is demonstrated (Preacher & Hayes, 2004). Especially with small sample

sizes, recent research supports the use of the bootstrapped samples and associated confidence interval to determine significance as opposed to sole use of the Sobel test compared with the normal distribution (Preacher & Hayes, 2004). Given that the proposed study used cross-sectional data, the mediational analyses do not support determining causal relationships.

Results
Preliminary Results

One-way analysis of variance and χ^2 tests found no significant differences between participants and nonparticipants based on demographic or medical factors. Multicollinearity diagnostics for multiple regression models did not reveal concerns with multicollinearity, with all tolerance values $\geq .2$ and all VIF values ≤ 3.

Descriptive Analyses and Correlational Results

Within the sample, adolescents were prescribed several classes of prescription medications including immunomodulators (58%), aminosalicylates (40%), corticosteroids (28%), proton pump inhibitors (35%), selective serotonin reuptake inhibitors (10%), antibiotics (10%), and others (e.g., antispasmodics, antihistamines, ulcer treatment, stool softeners; 35%). Parent report of attention problems was positively associated with parent report of conduct problems and parent and adolescent report of barriers to medication adherence and negatively associated with parent report of adherence. Parent report of conduct problems was positively associated with parent report of barriers to medication adherence and negatively associated with parent and adolescent report of adherence. Parent report of barriers was positively associated with adolescent report of barriers and negatively associated with both

parent and adolescent report of adherence. Finally, parent and adolescent reports of adherence were positively associated (Table II). Means, standard deviations, and ranges for all study variables appear in Table III. Although a clinical sample was not recruited, descriptive analyses revealed that two adolescents were rated as "at risk" and one adolescent was in the "clinically significant" range for attention difficulties on the BASC-2. One participant was rated as "at risk" for conduct problems.

Table III. *Means, Standard Deviations, and Ranges for Study Variables*

Variable	M (SD)	Observed range
Adolescent report		
Adherence: prescription medications	89.62% (14.44%)	25–100%
Barriers to adherence total	41.99 (11.65)	18.00–68.00
Parent report		
Adherence: prescription medications	92.83% (13.12%)	21–100%
BASC-2 attention problems[a]	48.91 (8.32)	35–72
BASC-2 conduct problems[a]	45.12 (5.57)	38–62
Barriers to adherence total	39.08 (9.90)	18.00–65.00
Disease Frustration/Adolescent Issues	18.39 (4.82)	7.00–30.00
Regimen Adaptation/Cognitive Issues	11.73 (4.15)	5.00–22.00
Ingestion Issues	17.73 (4.82)	7.00–29.00
Parent Reminder	2.61 (1.34)	1.00–5.00

Note. BASC-2 = Behavior Assessment System for Children—Second Edition
[a]Scores are scaled to a *T*-score metric based on the normative sample in the BASC-2 manual, such that the mean for the normative samples is 50, and the standard deviation is 10.

Table II. *Intercorrelations Among Study Variables*

Variables	1	2	3	4	5	6	7	8	9	10
1. BASC-2 attention problems	–	.41**	.41**	.35**	.32**	.36**	.26*	.30**	−.24*	−.12
2. BASC-2 conduct problems		–	.37**	.24*	.40**	.20	.32**	.19	−.33**	−.28**
3. Barriers to adherence total: parent report			–	.85**	.83**	.81**	.55**	.49**	−.40**	−.30**
4. Disease Frustration/Adolescent Issues: parent report				–	.50**	.85**	.31**	.56**	−.24*	−.25*
5. Regimen Adaptation/Cognitive Issues: parent report					–	.41**	.61**	.29**	−.51**	−.34**
6. Ingestion Issues: parent report						–	.18	.52**	−.11	−.12
7. Parent Reminder: parent report							–	.24*	−.34**	−.29**
8. Barriers to adherence total: adolescent report								–	−.09	−.16
9. Adherence: Parent report									–	.74**
10. Adherence: Adolescent report										–

Note. BASC-2 = Behavior Assessment System for Children—Second Edition.
*p ≤ .05, **p ≤ .01.

Do Barriers Account for the Relationship Between Attention Problems and Adherence?

We tested whether parent-reported barriers using the PMBS total score mediated the effect between attention problems and parent-reported adherence. The total effect of attention problems on adherence was significant (B = −.0038, SE = 0.0017, p < .05), as was the effect of attention problems on barriers (B = .4838, SE = 0.1194, p < .001) and the effect of barriers on adherence (B = −.0049, SE = 0.0015, p < .01). The effect of attention problems on adherence became nonsignificant when barriers were included in the model (B = −.0015, SE = 0.0017, p = .40). The Sobel test of the indirect effect, which directly assesses whether the total effect of attention problems on adherence is reduced by the addition of barriers to the model, was significant, and indicated mediation (z = −.0024, p = .01). Using 5,000 bootstrapped samples, the estimate of the indirect effect again indicated mediation, with a point estimate of −0.0024 (SE = 0.0009; 95% confidence interval [CI] = −0.0043 to −0.0007).

Given that the PMBS total score served as a mediator of the relationship between attention problems and adherence, we sought to determine whether specific subscales of the PMBS served as mediators by using a multiple mediator model. Determining whether specific subscales serve as mediators in addition to the total score may help to inform treatment intervention. We tested a model in which the four subscales of the PMBS served as mediators

for the relationship between attention problems and parent-reported adherence (Figure 1). As would be expected based on analyses using the total score, the total indirect effect of the four barriers subscales mediated the effect. At the subscale level, only Regimen Adaptation/Cognitive Issues served as a significant mediator, with a point estimate of −0.0025 (SE = 0.0014; 95% CI = −0.0061 to −0.0004). The total model accounted for 30% of the variance in parent-reported adherence (R² = .30, p < .001).

Parent-reported barriers were not found to mediate the relationship between attention problems and adolescent-reported adherence using tests of the indirect effects.

Do Barriers Account for the Relationship Between Conduct Problems and Adherence?

We tested whether parent-reported barriers using the PMBS total score mediated the effect between conduct problems and parent-reported adherence. The total effect of conduct problems on adherence was significant (B = −.0077, SE = 0.0024, p < .01), as was the effect of conduct problems on barriers (B = .6540, SE = 0.1814, p < .001) and the effect of barriers on adherence (B = −.0044, SE = 0.0014, p < .01). The effect of conduct problems on adherence became marginally significant when barriers were included in the model (B = −.0048, SE = 0.0025, p = .06). The Sobel test of the indirect effect was significant, indicating mediation (z = −.0028, p < .05). Using 5,000 bootstrapped samples, the estimate
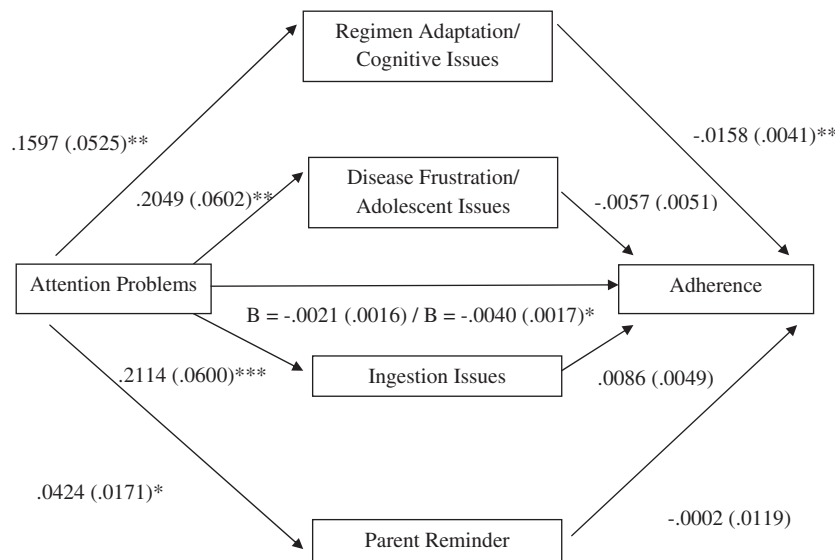

Figure 1. Parent-reported Regimen Adaptation/Cognitive Issues mediate the relationship between attention problems and parent-reported adherence. Path values represent unstandardized regression coefficients. Standard errors are in parentheses. Values before the slash represent the direct effect of attention problems on adherence with the inclusion of the mediating variables. Values after the slash represent the total effect of attention problems on adherence without the inclusion of the mediator. *p < .05, **p < .01, ***p < .001.
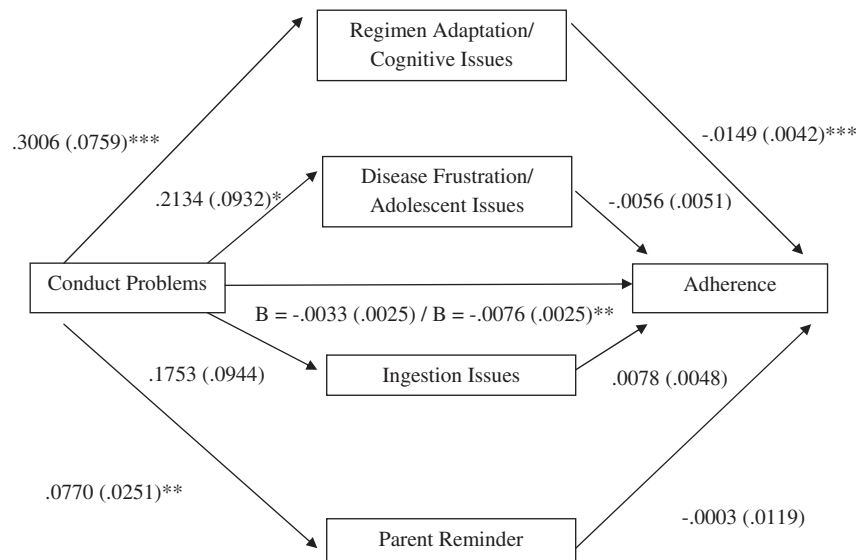
Figure 2. Parent-reported Regimen Adaptation/Cognitive Issues mediate the relationship between conduct problems and parent-reported adherence. Path values represent unstandardized regression coefficients. Standard errors are in parentheses. Values before the slash represent the direct effect of conduct problems on adherence with the inclusion of the mediating variables. Values after the slash represent the total effect of conduct problems on adherence without the inclusion of the mediator. *$p < .05$, **$p < .01$; ***$p < .001$.

of the indirect effect again suggested mediation, with a point estimate of -0.0028 ($SE = 0.0012$; 95% CI $= -0.0054$ to -0.0008).

Similar to analyses with parent-reported attention problems, we tested a model in which the four subscales of the PMBS served as mediators for the relationship between conduct problems and parent-reported adherence (Figure 2). As would be expected based on analyses using the total score, the total indirect effect of the four barriers subscales mediated the effect between conduct problems and adherence. At the subscale level, only the Regimen Adaptation/Cognitive Issues subscale served as a significant mediator, with a point estimate of -0.0046 ($SE = 0.0022$; 95% CI $= -0.0099$ to -0.0012). The total model accounted for 31% of the variance in parent-reported adherence ($R^2 = .31$, $p < .001$).

We sought to cross-replicate our findings by examining whether parent-reported barriers using the PMBS total score mediated the relationship between conduct problems and adolescent-reported adherence. The total effect of conduct problems on adherence was significant (B $= -.0073$, $SE = 0.0027$, $p < .01$), as was the effect of conduct problems on barriers (B $= .6515$, $SE = 0.1838$, $p < .001$) and the effect of barriers on adolescent-reported adherence (B $= -.0033$, $SE = 0.0016$, $p < .05$). The effect of conduct problems on adherence became nonsignificant when barriers were included in the model (B $= -.0051$, $SE = 0.0029$, $p > .05$). The Sobel test of the indirect effect was nonsignificant when using a normal distribution

($z = -.0021$, $p = .09$). Using 5,000 bootstrapped samples, however, the estimate of the indirect effect supported mediation, with a point estimate of -0.0021 ($SE = 0.0013$; 95% CI $= -0.0050$ to -0.0002). The model accounted for 12% of the variance in adolescent-reported adherence ($R^2 = .12$, $p < .01$). Only the total score served as a mediator, and no individual subscales served as mediators.

Do Barriers Account for the Relationship Between Attention Problems, Conduct Problems, and Adherence?

Finally, we tested whether parent-reported barriers using the PMBS total score mediated the effect between attention problems and conduct problems and parent-reported adherence when attention and conduct problems were combined in a single model (Figure 3). For the relationship between conduct problems and adherence, the estimate of the indirect effect indicated mediation, with a point estimate of -0.0018 ($SE = 0.0011$; 95% CI $= -0.0042$ to -0.0001). Although the direct effect of attention problems was not significant, evidence of an indirect effect through barriers was found, with a point estimate of -0.0015 ($SE = 0.0008$; 95% CI $= -0.0033$ to -0.0003). Although nonsignificant in the combined model, the relationship between attention problems and adherence (-0.0020) became smaller after controlling for barriers (-0.0005). Attention and conduct problems accounted for 12% of the variance in adherence ($R^2 = .12$, $p < .01$), and the total model with the inclusion of barriers accounted for
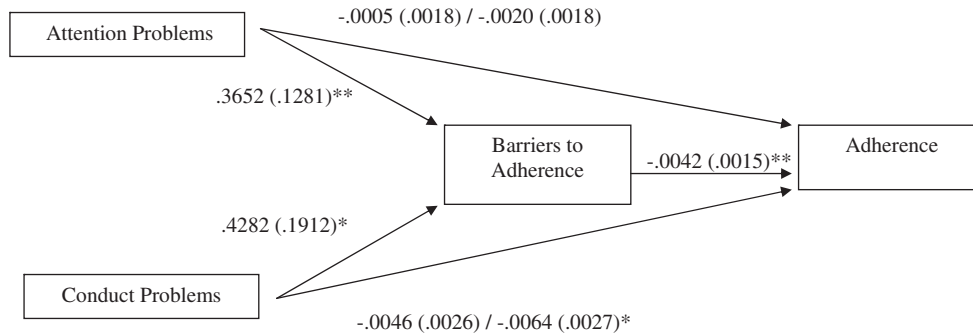
Figure 3. Parent-reported barriers to adherence mediate the relationship between attention and conduct problems and parent-reported adherence. Path values represent unstandardized regression coefficients. Standard errors are in parentheses. Values before the slash represent the direct effect of attention and conduct problems on adherence with the inclusion of the mediating variable. Values after the slash represent the total effect of attention and conduct problems on adherence without the inclusion of the mediator. *$p < .05$; **$p < .01$.

20% of the variance in parent-reported adherence ($R^2 = .20$, $p < .001$). No individual subscales of the PMBS served as mediators.

Parent-reported barriers were not found to mediate the relationship between attention problems, conduct problems, and adolescent-reported adherence using tests of the indirect effects.

Owing to the lack of a correlational relationship between adolescent-reported barriers and parent- or adolescent-reported adherence, mediation cannot exist and was therefore not modeled.

Would the Interaction Between Barriers and Attention/Conduct Problems Better Account for Adherence?

Given the cross-sectional nature of the data, causal relationships cannot be inferred from the previous mediation analyses. Inability to infer causality raises questions of whether moderated models would better explain the relationship between adherence, barriers, and attention/conduct problems. To answer this, three exploratory moderated models corresponding to the aforementioned mediation models were tested using mean centered variables. The models tested whether adolescent attention or conduct problems moderated the relationship between barriers and adherence.

In the first model, parent-reported adherence was regressed on the interaction between parent-reported barriers and attention problems. This model did not support a moderated relationship, evidenced by a nonsignificant interaction term ($t(81) = -1.47$, $p = .15$). In the second model, parent-reported adherence was regressed on the interaction between parent-reported barriers and conduct problems. This model also failed to support a moderated relationship, with a nonsignificant interaction term

($t(81) = -1.01$, $p = .32$). Finally, adolescent-reported adherence was regressed on the interaction between parent-reported barriers and conduct problems. Support for a significant interaction was not found ($t(81) = -.69$, $p = .49$). In sum, support was not found for attention or conduct problems moderating the relationship between barriers and adherence.

Discussion

Given the negative consequences associated with non-adherence in youth with IBD, the present study sought to examine associations between potentially modifiable behavioral functioning and medication adherence, with specific interest in the mediational role of barriers to adherence. At the bivariate level, levels of attention and conduct symptoms related to both parent- and adolescent-reported adherence, which builds on work with adolescent kidney transplant recipients indicating a relationship between child behavior and attention problems and lower adherence (Gerson et al., 2004). In the current study, higher levels of attention symptoms were negatively related to parent report of adherence and positively related to both parent and adolescent report of barriers to adherence. Symptoms of conduct problems (e.g., rule breaking, lying) negatively related to parent- and adolescent-reported adherence and positively related to parent-reported barriers.

To better understand the mechanism by which behavioral functioning was associated with adherence, mediational analyses were conducted. When levels of attention problems were examined, parent-reported barriers mediated the relationship with parent-reported, but not adolescent-reported, adherence. However, parent-reported barriers mediated the relationship between levels of

conduct problems and both parent- and adolescent-reported adherence. Finally, the indirect effect through barriers was supported when attention problems and conduct problems were both included in the same model. In other words, increased barriers explained the relationship between higher levels of attention and conduct problems and adherence in the current sample. Our results suggest that higher levels of attention and conduct problems predict poorer adherence through barriers even when scores do not reach clinically significant cutoffs. To best conceptualize factors related to adherence, practitioners should assess individual barriers as well as behavioral functioning and whether a patient's behavior, including mild difficulties with attention or conduct, may be interfering with adherence. The mediational relationship with parent-reported conduct problems and barriers and adolescent-reported adherence supports the validity of the findings and suggests that reporter variance cannot be assumed to be responsible for the body of findings.

After documenting that the total scale score of the PMBS mediated the relationship between behavioral functioning and adherence, we sought to add specificity to our findings by investigating whether subscales of the PMBS would also serve as mediators. Interestingly, one subscale, Regimen Adaptation/Cognitive Issues, emerged as significant in the models predicting parent-reported adherence from attention problems and conduct problems separately, although all PMBS subscales except for Ingestion Issues were related to parent and adolescent report of adherence at the bivariate level. Although other barriers are related to adherence, barriers loading on the Regimen Adaptation/Cognitive Issues subscale account for the most variance in adherence and are an important area for future research. Regimen Adaptation/Cognitive Issues includes forgetfulness, poor organization, being busy, relying on a parental reminder, and poor planning. These barriers are face valid as to the types of barriers we would expect youth with higher levels of conduct and, especially, attention symptoms to experience when attempting to manage a complicated medication regimen.

Similar to previously published research, we found a relationship between high levels of barriers and poorer medication adherence (Greenley et al., 2010; Ingerski et al., 2010). Unexpectedly, however, we did not find a relationship between adolescent-reported barriers and adherence. It may be that parents were more adept at recognizing barriers that their adolescents experience, or that adolescents were less willing to acknowledge barriers. Our hypotheses regarding a significant relationship between parent report of more barriers and poorer adherence were supported. Identified barriers may be a point of

intervention for youth with symptoms of attention or conduct problems who also experience medication nonadherence. For example, an adolescent with higher levels of attention problems might experience most difficulty with forgetting doses or planning ahead for a sleepover by packing extra doses. Assessment in an adolescent with symptoms of conduct problems might reveal defiance related to the medical regimen or medication refusal. Results suggest that targeted interventions to address barriers may be an effective treatment option for nonadherence in youth with IBD. To address Regimen Adaptation/Cognitive barriers, practitioners may help patients increase structure within the home such as a daily medication schedule or the use of a physical reminder such as a pillbox. Patients may also benefit from automatic prescription medication refill reminders. Technology offers several solutions to difficulties with forgetting or poor organization, including automatic text message reminders for cell phones. Further intervention work is needed, however, to test the development and implementation of such interventions.

Given the significant associations found with parent-reported barriers, adolescents may benefit most when both parent and adolescent report of barriers to adherence are obtained. Reliance on the adolescent's report alone may not be sufficient for identifying and addressing barriers that youth with greater attention and conduct problems experience. Use of both parent and adolescent reports can be used to guide collaborative discussion between parent and child on barriers that can be addressed and the most effective ways to do so at a family systems level.

Interpretation of these data must be done in light of study limitations. First, the sample of youth with IBD under examination was high functioning, demonstrating relatively high levels of self- and proxy-reported medication adherence and primarily normative behavioral functioning. As a result, caution must be taken when generalizing results to youth with greater nonadherence and behavioral difficulties. Although findings may not readily generalize to youth with diagnosable levels of attention and conduct problems, results suggest that even nonclinical levels of attention and conduct problems that would be deemed "normal" when measured categorically may be a risk factor for poorer adherence. Second, the mediation models yielded small effect sizes. Given our past research demonstrating relationships between adherence and more traditionally studied disease, family, and individual factors (Reed-Knight, Lewis, & Blount, 2011), however, we sought to examine the contribution of less often studied individual-difference factors, including symptoms of attention and conduct problems and barriers. Although the

demonstrated effect sizes are quantitatively small, results are meaningful in terms of suggesting that everyday behavioral functioning may relate to levels of adherence in youth with IBD. The use of mediational analyses should not be used to infer causation. The current study used cross-sectional data that prevents the inference of directionality. Longitudinal research is needed to test causal relationships between behavioral problems, barriers, and adherence. The sample was primarily middle to high income, Caucasian, and limited to adolescents, which limits generalizability to youth with IBD from different ethnicities, income levels, and ages. The current sample is demographically similar in terms of ethnicity and income, however, to previous research on adolescents with IBD and is likely influenced by the fact that Caucasians are disproportionately diagnosed with IBD (Hommel et al., 2009). Next, only self- and parent reports of adherence were used, which may indicate higher levels of adherence relative to more objective methods of assessment (Hommel et al., 2009).

The current study identified risk factors for nonadherence in youth with IBD, including higher levels of attention and conduct problem symptoms and barriers. Parent-reported barriers explained the relationship between levels of attention problems and parent-reported adherence as well as levels of conduct problems and parent- and adolescent-reported adherence. Interventions to target barriers may include problem solving, planning ahead, cuing strategies, and communication skills. Clinically, results suggest that everyday behavioral functioning may help identify adolescents with IBD at risk for nonadherence who may benefit from assessment and treatment to target individually identified barriers.

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