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Profile of Depression in Adolescents with Inflammatory Bowel Disease: Implications for Treatment

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Abstract

Background—The purpose was to determine the utility of including neurovegetative symptoms in assessments of depression in youth with inflammatory bowel disease (IBD).

Methods—Forty-one youth with IBD and concurrent depressive symptomatology were enrolled in an intervention trial and received either 9 modules of cognitive-behavioral therapy (PASCET-PI) or treatment as usual (TAU). Youth and their primary caregivers completed the Children's Depression Inventory (CDI) at pre- (T1) and posttreatment (T2). Disease severity measures and current steroid dosage were obtained at each timepoint. Change in the individual items of the CDI was compared across groups and examined in association with change in physical illness course.

Results—Paired sample *t*-tests revealed significant changes in CDI item scores from T1 to T2 for a majority of the depressive symptoms assessed in the PASCET-PI group, but not for the TAU group. These changes did not appear to be linked to changes in disease severity and/or steroid dosage across these same timepoints.

Conclusions—The inclusion of somatic items in the assessment of depression in physically ill youth is important, as these symptoms seem to respond to psychotherapeutic intervention. The present results would suggest that improvements in depressive symptomatology are not solely related to improvements in the course of IBD and that these items do reflect an important part of the profile of depressive symptoms in youth with IBD. Future research is warranted to replicate present findings and explore the generalizability of these results to other pediatric illness populations.

Keywords

inflammatory bowel disease; depression; Children's Depression Inventory

An unresolved problem in pediatric medicine is how to ascertain whether a symptom (e.g., fatigue) is related to a physical illness (e.g., diarrhea in inflammatory bowel disease [IBD]) or an indicator of psychiatric comorbidity, particularly depression. Two strategies utilized in studies of adults with physical illness have been to exclude patients with the most severe physical illness activity (medically hospitalized) and/or eliminating items on the depressive measures utilized that are more prevalent in patients with a specific physical illness.^{1,2} More

recent studies examining depression in physically ill populations have shown that using the entire depressive screen instrument is more valid (e.g., multiple sclerosis,^{3,4} diabetes,⁵ cancer,^{6,7} and depression induced by interferon treatment⁸). Finally, several studies have shown that such depressive/“sickness” symptoms respond to psychiatric treatment regardless of their etiology.^{7,8} Such inclusive approaches have been validated in physically ill adults but not in pediatric populations. This study will characterize depression in a pediatric physically ill population to assess if individual depressive symptoms, including the neurovegetative ones, respond to psychosocial intervention using IBD as a model illness.

Ulcerative colitis (UC) and Crohn's disease (CD), collectively described as IBD, are challenging gastrointestinal disorders that involve a number of painful and often disabling symptoms such as diarrhea, fever, severe abdominal pain, rectal bleeding, and extraintestinal inflammation. Understanding and coping with such physical challenges can be particularly difficult for youth with IBD, who report reduced health-related quality of life relative to physically healthy peers.⁹ Research has also shown that youth with IBD are at increased risk for depression relative to physically healthy peers.¹⁰⁻¹³ Both the inflammatory processes underlying IBD as well as treatment with steroids have been implicated in the etiology of depression in this pediatric population.¹² Specifically, the cytokines released during inflammatory states can cause “sickness behaviors” that closely mirror or overlap symptoms of depression.¹⁴ Steroid-induced depression has been reported in several other depressive medically ill populations.¹⁵ Questions about the etiology of reported neurovegetative symptoms have important implications for treatment planning. If symptoms of physical illnesses such as IBD mimic depression, treatment of these depressive symptoms might not involve psychotherapeutic intervention but instead respond adequately to routine medical care for IBD.

As with adult self-report depression inventories, the use of child depression inventories in medical populations creates similar methodological challenges, as these measures often include a number of neurovegetative symptoms. For example, the Children's Depression Inventory (CDI),¹⁶ a widely used self-report measure that assesses depressive symptoms in children and adolescents, includes items assessing the following symptoms: sleep, appetite, fatigue, and concern about health. It is one of the most frequently used and well-validated measures of depressive symptoms, and has been used in a wide range of patient populations.^{16,17} However, research on the application of the CDI in medical populations is lacking, and thus, this study has 2 aims. Aim 1: This present study is the first, to our knowledge, to examine the sensitivity of depression scale items in pediatric IBD in the context of treatment for depression. Based on recent work in adults with multiple sclerosis,⁴ and youth with IBD,¹³ we anticipated that a majority of CDI items, including somatic items, would improve over the course of psychotherapeutic treatment. Aim 2: The present study sought to demonstrate that changes in the somatic items on the CDI following psychotherapeutic intervention cannot merely be attributed to changes in objective measures of disease status and/or severity. It was predicted that correlations between changes in the somatic items on the CDI would not be associated with changes in disease severity and/or steroid treatment.

MATERIALS AND METHODS

Participants

Participants were 41 adolescents ages 11–17, diagnosed with IBD and concurrent depressive symptomatology, as measured by the CDI and CDI-Parent Report (CDI-P) and confirmed by the KSADS-PL (see Ref. 13 for recruitment details).

Measures

Depressive Severity—The CDI and CDI-P were used to measure depressive severity. The CDI is a validated self-report measure of depressive severity.¹⁶ The CDI and CDI-P scores were summed to yield a total CDI severity score (CDI-CP), which served as the primary measure of depressive severity (range 9–42).

IBD Severity—Two well-validated IBD severity scales were used to measure illness severity: the Pediatric Crohn's Disease Activity Index (PCDAI)¹⁸ for CD and the Clinical Score of Kozarek¹⁹ for UC. Both well-validated IBD scales are based on clinical information from the medical chart and provide continuous and ranked categorical disease severity ratings. Although both scales rate a combination of signs and symptoms (e.g., abdominal pain, diarrhea, well-being), the PCDAI also includes physical findings and laboratory values. Only the categorical rating system (inactive, mild, and moderate/severe) was used because this allowed for pooling of the CD and UC data. Categorical disease severity was scored by two independent physician raters who were blinded to treatment status for all of the participants. Interrater reliability scores were 0.87 at T1 and 0.97 at T2. Exogenous steroid use and dose at the time of the assessments were obtained from the medical record.

Procedure

Participants were screened for the study using the CDI and CDI-P as part of a 2-step screening process. Eligible participants were randomized to receive either 9 modules of a manual-based cognitive-behavior treatment (Primary and Secondary Control Enhancement Therapy-Physical Illness: PASCET-PI)²⁰ or treatment as usual (TAU) including a written sheet for parents about the warning signs of major depression and available treatment options.²¹ Participants were assessed for depressive symptomatology before PASCET-PI or TAU began (T1), and 12–14 weeks from T1 (T2), at which time individuals in the PASCET-PI group had completed the intervention. More detailed information about the screening procedures and treatment are published elsewhere.¹³

Data Analytic Strategy

Analyses were conducted separately on individuals who received the PASCET-PI intervention versus those who received TAU. CDI and CDI-P scores were combined to form the CDI-CP in order to maximize power, consistent with previous work with this sample.¹³ Changes in all CDI-CP item scores from T1 and T2 were analyzed using paired-sample *t*-tests to determine item-level effects of psychotherapeutic intervention. Additionally, bivariate Spearman correlations were run to investigate associations between CDI-CP change scores, generated from T1 and T2 CDI-CP item level responses, and T1-T2 change scores for both disease severity and steroid dosage.

RESULTS

Subject Characteristics

Forty-one participants were randomized to either the PASCET-PI group ($N = 22$) or the TAU group ($N = 19$). The mean age was 14.99 years ($SD = 2.01$), with 51% female. Ethnic distribution was 78.1% white, 14.6% African American, 2.4% Hispanic, and 4.9% unspecified. At baseline, there was no difference between the 2 treatment groups in terms of age, sex, IBD type, IBD severity, or mean steroid dose. At T2, 15.4% of the PASCET-PI group and 25% of the comparison group still had moderate/severe disease activity ($N = 25$). The change in the score of IBD severity between the groups was not significant.

At T1, 12 participants in the PASCET-PI group (45%) and 10 participants in the TAU group (53%) met diagnostic criteria on the KSADS-PL for minor depression. The remainder met criteria for Adjustment Disorder with depressed mood. Mean CDI scores for the PASCET-PI group at T1 were as follows: CDI-C = 12.27, CDI-P = 13.95, CDI-CP = 26.24. Mean CDI scores for the TAU group at T1 were as follows: CDI-C = 9.84, CDI-P = 13.33, CDI-CP = 22.78. There were no significant differences between groups in levels of depressive symptoms at T1.¹³

T1-T2 Change in CDI-CP Item-level Response

Paired sample *t*-tests revealed that for the PASCET-PI group 19 of the 27 CDI-CP items (70.37%) showed statistically significant decreases (indicating reductions in depressive symptoms), with the remainder of the items showing decreases that were not statistically significant. For the TAU group, only 4 of the 27 CDI-CP items (14.81%) showed statistically significant improvement. Moreover, 4 of the CDI-CP items (crying, concern about health, difficulty enjoying school, and not getting along with others) showed increases from T1-T2 in the TAU group, suggesting worsening of symptoms, although these increases were nonsignificant.

With respect to CDI-CP items indexing somatic symptoms of depression (sleep problems, fatigue, poor appetite, concern about health), in the PASCET-PI group each of these symptoms showed statistically significant improvement, while only 1 of these symptoms showed statistically significant improvement in the TAU group (poor appetite). Neither group evidenced a statistically significant improvement in the item assessing suicidal ideation, but it should be noted that this item was infrequently endorsed at both timepoints, regardless of group assignment (Table 1).

Correlations Between T1-T2 Change in CDI-CP Item Scores and Change in Disease Severity and Steroid Dosage

With respect to disease severity, for the PASCET-PI group a change in CDI-CP item scores from T1 to T2 was correlated with a change in disease severity for only 1 of the CDI-CP items: feeling alone. It should be noted that change in disease severity was not associated with T1-T2 change in any of the somatic items on the CDI-CP. For the TAU group there was one significant correlation between T1-T2 change in CDI-CP item responses and change in disease severity, for the item assessing feelings about the future.

With respect to change in steroid dosage, for the PASCET-PI group a change in CDI-CP item scores from T1 to T2 was correlated with a change in steroid dosage for the following CDI-CP items: feeling sad, blaming self, sleep problems, and feeling inadequate relative to others. For the TAU group there were significant associations between change in steroid dosage and T1-T2 change in the following two CDI-CP items: anhedonia and feeling inadequate relative to others (Table 2).

DISCUSSION

These results demonstrate that 19 out of 27 items on the CDI (70.37%), including all of the items assessing somatic symptoms, showed improvement following manualized CBT for depression in youth with IBD. The number of symptoms that significantly improved in the group of youth receiving TAU was far fewer, with only 4 of 27 symptoms (14.81%) improving from T1 to T2. These results suggest that excluding somatic items on the CDI may result in failure to capture important depressive symptoms that respond to psychotherapeutic treatment in youth with IBD. Further, almost none of the change scores for items on the CDI in the PASCET-PI group, including change scores for somatic items, were significantly correlated

with changes in disease severity or changes in steroid treatment, suggesting that the improvement in depressive symptoms was reflective of a response to CBT rather than changes in disease course or the effects of steroid medication. Thus, it appears that including the items of the CDI that assess somatic symptoms is important to obtain an accurate and comprehensive picture of depressive symptomatology in youth with IBD. The study results are consistent with recent work in adults with multiple sclerosis investigating the utility of including somatic items when screening for depression.⁴

It should be noted that a change in several of the CDI-CP items was associated with changes in physical functioning (either improvements in disease severity or reduction in steroid dosage) in both the PASCET-PI and TAU groups. While some might argue that this lends credence to claims that elevated depression scores in physically ill populations are merely a manifestation of the overlap between physical symptoms of disease and somatic symptoms of depression (suggesting psychotherapeutic intervention might not be warranted), it should be noted that within the PASCET-PI group in only one case was this T1-T2 change in disease severity (specifically, decreased steroid dosage) associated with change in a somatic item on the CDI-CP (sleep disturbance). Improvements in all other somatic assessed by the CDI-CP were not associated with objective improvements in physical functioning in either the PASCET-PI or TAU groups. In conjunction with the failure to demonstrate associations between changes in disease severity and changes in CDI-CP item scores more broadly, this would suggest that it was not improvements in physical functioning alone that were responsible for improvements in depressive symptoms. This PASCET-PI intervention, however, was effective in significantly improving global functioning in youth over this 3-month intervention period in youth with both mild and more significant depression.^{12,13}

Interestingly, a change in some CDI-CP items was negatively correlated with a change in disease severity and changes in steroid treatment for the PASCET-PI group and not for the TAU group. Specifically, in the PASCET-PI group, increases in IBD symptoms at T2 (as indexed by higher disease severity ratings and increases in steroid dosage) were associated with improvement in sadness and feeling alone (see Table 2). This association may indicate a protective role of the cognitive behavioral intervention such that even with worsening physical functioning, children in the PASCET-PI group sustained improvements in these depressive symptoms.

Several limitations affect the generalizability of these findings. First, the CDI is a brief screening instrument and is affected by the same limitations as other self-report measures (e.g., socially desirable responding). Second, the study did not include a physically healthy, depressed comparison group. Inclusion of this group would clarify whether our results reflected patterns of response to treatment that are unique to IBD or a typical response to treatment for depression. Third, no corrections to control type I error were utilized, with the decision to err on the side of detecting versus not detecting differences in this study. Fourth, this sample was small in size, and a larger sample might have produced even more pronounced differences between groups. Fifth, the sample was a nonreferred clinical sample with only mild/moderate depression, limiting the generalizability of findings to a more severely depressed sample. Finally, the sample was primarily a Caucasian sample, and thus, generalizability to other ethnic groups is limited.

Despite its limitations, the present study adds to the extant literature debating the utility of including somatic items in assessments of depression in physically ill populations and represents a first step toward understanding this question in pediatric populations. These findings suggest that not only do somatic symptoms of depression show significant improvements in response to cognitive-behavioral treatment (relative to a TAU control group), but these improvements are more than a byproduct of improved physical functioning.

Moreover, this work lends support to a promising psychotherapeutic intervention that in some cases improved emotional functioning even in the context of decreased physical health. Future work utilizing larger samples, with more detailed assessments of depressive symptoms (e.g., structured interviews), will add strength to these findings. Moreover, subsequent work in other physically ill pediatric populations should be conducted to determine whether these results can be generalized to other illness populations, as these concerns are not specific to youth with IBD.

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TABLE 1
CDI Item Level Responses at T1 and T2 by Treatment Condition

Item	Description	PASCET-PI Group					TAU Group				
		T1		T2		t (df)	T1		T2		t (df)
		Mean	(SD)	Mean	(SD)		Mean	(SD)	Mean	(SD)	
CDI-1	Feels sad	0.95	(0.85)	0.11	(0.32)	4.09 (18)***	0.53	(0.70)	0.26	(0.73)	1.32 (18)
CDI-2	Discouraged about the future	1.42	(1.07)	0.47	(0.51)	4.53 (18)***	1.47	(0.96)	0.84	(0.69)	2.19 (18)*
CDI-3	Feels like a failure	0.32	(0.48)	0.05	(0.23)	2.54 (18)*	0.26	(0.45)	0.16	(0.37)	0.81 (18)
CDI-4	Anhedonia	1.21	(0.79)	0.63	(0.76)	3.01 (18)**	1.21	(0.79)	1.16	(0.76)	0.22 (18)
CDI-5	Has behavior problems	0.37	(0.76)	0.05	(0.23)	1.68 (18)	0.29	(0.59)	0.12	(0.49)	1.14 (16)
CDI-6	Worries about the future	0.89	(0.96)	0.17	(0.38)	3.20 (17)**	1.24	(0.83)	0.47	(0.72)	3.25 (16)**
CDI-7	Dislikes self	0.42	(0.51)	0.21	(0.54)	1.71 (18)	0.59	(0.71)	0.24	(0.44)	1.69 (16)
CDI-8	Blames self	0.74	(0.56)	0.21	(0.42)	3.75 (18)***	0.47	(0.70)	0.21	(0.42)	1.32 (18)
CDI-9	Suicidal ideation	0.05	(0.23)	0.05	(0.23)	0.00 (18)	0.17	(0.38)	0.00	(0.00)	1.84 (17)
CDI-10	Crying	0.63	(0.68)	0.00	(0.00)	4.03 (18)***	0.29	(0.69)	0.41	(1.00)	-0.57 (16)
CDI-11	Feels bothered by things	1.58	(1.22)	0.47	(0.70)	4.38 (18)***	1.17	(0.79)	0.83	(0.79)	1.68 (17)
CDI-12	Losing interest in others	0.74	(0.93)	0.32	(0.75)	3.02 (18)**	0.39	(0.50)	0.72	(0.75)	-1.56 (17)
CDI-13	Indecisive	1.32	(0.95)	0.42	(0.61)	4.16 (18)***	1.44	(1.34)	1.28	(1.02)	0.82 (17)
CDI-14	Dislikes physical appearance	1.32	(1.16)	0.58	(0.84)	2.93 (18)***	1.39	(1.04)	1.00	(0.69)	1.69 (17)
CDI-15	Not motivated to do schoolwork	1.58	(1.35)	1.26	(1.05)	1.24 (18)	1.28	(1.27)	1.06	(0.80)	1.17 (17)
CDI-16	Sleep problems	1.33	(1.24)	0.72	(1.18)	2.65 (17)*	1.39	(1.29)	1.17	(1.42)	0.64 (17)
CDI-17	Fatigue	2.00	(0.94)	0.84	(1.02)	4.98 (18)*****	1.50	(0.92)	1.39	(1.20)	0.49 (17)
CDI-18	Poor appetite	0.89	(1.20)	0.21	(0.42)	2.39 (18)*	1.56	(1.46)	0.78	(0.88)	2.12 (17)*
CDI-19	Concerned about health	1.26	(0.99)	0.47	(0.70)	3.03 (18)**	1.22	(0.88)	1.28	(1.02)	-0.21 (17)
CDI-20	Feels alone	0.68	(0.82)	0.21	(0.54)	3.38 (18)**	0.83	(0.71)	0.61	(0.92)	1.00 (17)
CDI-21	Difficulty enjoying school	1.68	(1.06)	1.11	(1.15)	1.77 (18)	1.29	(1.10)	1.29	(1.21)	0.00 (16)
CDI-22	Does not have friends	0.89	(0.94)	0.74	(0.65)	1.14 (18)	0.78	(0.65)	0.67	(0.84)	0.81 (17)
CDI-23	Has declining grades	1.00	(0.84)	0.39	(0.78)	2.65 (17)*	0.72	(1.02)	0.50	(0.62)	1.17 (17)
CDI-24	Feels inadequate relative to others	1.11	(0.88)	0.58	(0.77)	2.54 (18)*	1.00	(1.00)	0.71	(0.85)	1.43 (16)

Item	Description	PASCET-PI Group						TAU Group			
		T1			T2			T1		T2	
		Mean	(SD)	<i>t</i> (df)	Mean	(SD)	<i>t</i> (df)	Mean	(SD)	Mean	(SD)
CDI-25	Does not feel loved	0.58	(0.90)	0.16	(0.50)	2.04 (18)		0.29	(0.47)	0.00	(0.00)
CDI-26	Does not follow the rules	0.68	(0.89)	0.26	(0.56)	2.19 (18)*		0.50	(0.71)	0.39	(0.61)
CDI-27	Does not get along with others	0.42	(0.61)	0.26	(0.56)	0.90 (18)		0.11	(0.32)	0.33	(0.77)

* $P < 0.05$

** $P < 0.01$

*** $P < 0.001$

**** $P < 0.0001$.

TABLE 2
Correlations Between Change in CDI-CP Scores and Disease Activity

CDI-CP Item	PASCET-PI		TAU		
	Disease Severity	Steroid Dosage	Disease Severity	Steroid Dosage	
CDI-1	Feels sad	-0.38	-0.47*	0.09	0.32
CDI-2	Discouraged about the future	-0.24	0.02	0.71**	0.31
CDI-3	Feels like a failure	-0.43	0.27	-0.05	-0.09
CDI-4	Anhedonia	0.47	0.38	0.42	0.56*
CDI-5	Has behavior problems	0.22	-0.41	-0.06	0.28
CDI-6	Worries about the future	0.00	-0.22	0.36	0.29
CDI-7	Dislikes self	-0.31	-0.21	0.02	0.04
CDI-8	Blames self	-0.59	0.51*	0.35	0.13
CDI-9	Suicidal ideation	-0.51	-0.03	0.00	-0.16
CDI-10	Crying	-0.15	0.28	0.20	0.43
CDI-11	Feels bothered by things	0.06	0.00	-0.07	0.35
CDI-12	Losing interest in others	0.27	-0.26	0.05	-0.03
CDI-13	Indecisive	0.33	-0.17	-0.05	-0.30
CDI-14	Dislikes physical appearance	-0.17	0.11	0.40	0.19
CDI-15	Not motivated to do schoolwork	0.25	0.21	-0.24	-0.23
CDI-16	Sleep problems	0.44	0.56*	0.24	0.34
CDI-17	Fatigue	-0.28	0.42	0.26	0.43
CDI-18	Poor appetite	0.44	0.33	0.47	0.22
CDI-19	Concerned about health	-0.49	0.42	0.43	0.34
CDI-20	Feels alone	-0.61*	-0.07	0.20	0.06
CDI-21	Difficulty enjoying school	-0.05	0.00	0.09	0.15
CDI-22	Does not have friends	-0.08	-0.38	0.55	-0.16
CDI-23	Has declining grades	-0.18	-0.19	0.15	0.29
CDI-24	Feels inadequate relative to others	0.24	0.59**	-0.06	0.53*
CDI-25	Does not feel loved	-0.49	0.11	-0.23	-0.22
CDI-26	Does not follows the rules	-0.17	0.18	0.44	-0.25
CDI-27	Does not get along with others	-0.34	-0.17	0.30	-0.11
Total CDI Score		-0.13	0.31	0.62	0.47

CDI-CP Item	PASCET-PI		TAU	
	Disease Severity	Steroid Dosage	Disease Severity	Steroid Dosage
* $P < 0.05$				
** $P < 0.01$.				