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Negative emotions in irritable bowel syndrome: which differences among IBS subtypes?

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Abstract

There are conflicting data on peculiar negative emotional patterns in Irritable Bowel Syndrome subtypes. Our study was aimed to determine possible differences in depression, anxiety and anger in patients suffering from Irritable Bowel Syndrome constipation, diarrhoea and mixed subtypes. The sample underwent a psychometric examination for the assessment of depression

(Hamilton Rating Scale Depression), anxiety (Hamilton Rating Scale Anxiety), and anger (State-Trait Anger Expression Scale 2). Differences among groups were assessed using the Analysis of variance with Bonferroni post hoc comparisons, or the χ^2-test if requested.

111 subjects (diarrhoea subtype =37; constipation subtype=34; mixed subtype=40) were included in the study. The severity of depressive symptoms was "moderate" in patients with constipation subtype and "mild" in patients with diarrhoea and mixed subtypes (17.15±6.7 vs 14.24±6.6 vs 12.50±4.9); no statistically significant differences were documented among subtypes. Severity of anxiety symptoms was "mild to moderate" in patients with constipation subtype (mean = 18.53 ± 7.7), and mild in patients with diarrhoea (mean = 13.35 ± 7.1) and mixed subtypes (mean = 13.25 ± 4.7); statistically significant differences among subgroups were found (Constipation vs Diarrhoea: p=0.004; Constipation vs Mixed: p=0.003). Regarding anger, significant differences among subgroups emerged at State Anger Feeling Angry and Anger In variables, both higher in constipation subtype group than in mixed subtype group (State Anger Feeling Angry: p=0.002; Anger In: p=0.001). Results showed that IBS-C patients were characterized by higher levels of anxiety than the other two subgroups, and that a consistent number of subjects from the IBS-C subgroup had anxiety scores within the pathological range. Furthermore, IBS-C patients showing a trend to experience more depressive symptoms than IBS-D and IBS-M patients.

Key words: Anger, anxiety, depression, Irritable Bowel Syndrome subtype, negative emotions

Introduction

Irritable bowel syndrome (IBS), a chronic, functional disorder of the gastrointestinal tract, characterised by abdominal pain, alterations in bowel habits (constipation and/or diarrhoea) and other minor symptoms (bloating, abdominal distension, feeling of incomplete evacuation and urgency), is the most commonly diagnosed gastrointestinal disorder, and its prevalence in the general population, ranging from 7% to 21%, is highly variable, depending on data collection,

samples recruitment, diagnostic criteria, and methodological differences (Sperber et al., 2016). According to the alteration of the stool patterns (frequency, consistency, straining, and urgency) three subtypes of IBS can be identified: constipation-predominant (IBS-C), determined by predominantly hard or lumpy stools ≥ 25% of the time with diarrhea criteria <25% of the time, diarrhea-predominant (IBS-D), characterized by predominantly loose or watery stools ≥25% of the time with constipation criteria <25% of the time, and mixed (IBS-M), meeting criteria for IBS-D and IBS-C ≥25% of time (Longstreth, Thompson, & Chey, 2006). IBS has a great impact on socio-relational and work functioning, and patients usually report significantly reduction of health-related quality of life and work productivity (Spiegel, 2009).

Although the pathogenesis of IBS remains incompletely understood, a growing amount of evidence supports the dysregulation and/or hyper-reactivity of the brain-gut axis (BGA), a framework involving bidirectional pathways among central nervous system (CNS), autonomic nervous system (ANS), and enteric nervous system (ENS), useful to understand the interplay among emotional and cognitive factors, psychopathology, and chronic distress as possible contributing factors or associated features in IBS onset, course, and clinical expression. IBS patients show dysfunctions in the BGA, including abnormalities in the autonomic nervous system, peripheral factors, central neural functions, neurotransmitters, hormones, and peptides (Camilleri, 2014; Mayer & Tillisch, 2011). Within this context, affective and emotional features are mostly viewed as specific and integral to the syndrome, rather than consequences of IBS, and the physiological effects of emotional arousal provide one potential mechanism by which affective and cognitive states may influence IBS pathophysiology. Emotional arousal mainly affects intestinal motility patterns and visceral pain sensitivity (Chapman & Martin, 2011; Walter et al., 2013), whereas persistent negative affective states and chronic psychological distress have been further associated with alterations of immune system and inflammatory pathways (Gao, 2013; Muscatello, Bruno, Scimeca, Pandolfo, & Zoccali, 2014; Scully et al.,2010).

Population and cohort studies have shown that IBS is consistently associated with psychopathology (Bengtson, Aamodt, Vatn, & Harris, 2015; Thijssen et al., 2010);

among individuals diagnosed with IBS, 27.5% also had a comorbid psychiatric mood or anxiety disorder, and among lifetime IBS, 50.5% also had a lifetime psychopathological condition (Mykletun et al., 2010). Whether psychopathological symptoms precede the onset of the disease or result from the symptoms of IBS is still not resolved, although the biopsychosocial model of illness and disease would suggest a bidirectional relationship (Engel, 1980). Regarding possible psychopathological differences in IBS subtypes, high rates of psychiatric comorbidity and history of sexual abuse were found in IBS-D patients (Guthrie et al., 2003), and depression severity was negatively correlated with rectal pain, but only in IBS-M subtype (de Medeiros et al., 2008). It has been suggested that IBS subtypes could represent entities that are to some extent biologically distinct, as shown by a recent study aimed to assess a combination of potential biomarkers, including a combination of gene expression, serological markers, and psychological factors; however, the Authors provided evidence that the incremental value of psychological measures was effective in differentiating IBS patients from healthy controls, whereas the same factors played a minimal role in subtype differentiation (Jones et al., 2014). In a previous study, we have shown that IBS-C patients had higher levels of negative emotions (depression, anxiety and anger) than IBS-D subjects (Muscatello et al., 2010); recently, disease severity in IBS-C was found to have moderate correlation with depression, although no further significant differences in terms of symptom severity, somatization, quality of life, and levels of anxiety emerged in IBS subtypes (Rey de Castro, Miller, Carruthers, & Whorwell, 2015). Moreover, in IBS-C, the degree of anxiety was significantly associated with abdominal discomfort, pain, and bloating (Kanazawa et al., 2016). However, other studies have not found a relationship between IBS symptoms and negative emotions (van der Veek, Van Rood, & Masclee, 2008), and actually there is no strong evidence about possible associations between IBS subtypes and peculiar emotional profiles.

Based on the conflicting evidence from the literature and starting from the hypothesis that IBS subtypes may have different emotional profiles and symptomatic expressions of negative emotions, the present study was aimed at

investigating possible differences in negative emotions in a sample of non-psychiatric IBS patients.

Materials and methods

Subjects and study setting

The accidental sampling method was used to recruit the participants in the current study. Adult patients (18-70 years old) referred to the Clinical Unit for Chronic Bowel Disorders and to the Digestive Endoscopy Unit of the University Hospital of Messina, fulfilling the Rome III criteria for IBS (Longstreth et al., 2006), were enrolled in the study after full evaluation by a gastroenterologist and colonoscopic examination. Rome III criteria for diagnosis of IBS include: recurrent abdominal pain or discomfort 3 days per month in the last 3 months associated with 2 or more of: symptom onset 6 months before diagnosis, improvement with defecation, onset associated with a change in frequency of stool, onset associated with a change in form of stool (Longstreth et al., 2006). Afterwards, they underwent a non-structured clinical interview conducted by a psychiatrist with at least five-years clinical experience in order to exclude the presence of concurrent psychiatric disorders. For the purpose of the study, participants were classified according to the predominant bowel habit alteration of IBS, as assessed by the Rome III criteria (Longstreth et al., 2006). Subject with unclassified stool pattern (IBS-U), defined when patients could not be subtyped according to Rome III criteria (Longstreth et al., 2006), an organic pathogenesis of the disease (a history of gastrointestinal surgery, gastrointestinal symptoms related to or exacerbated by consumption of milk or milk products), significant concurrent medical illnesses, organic brain disorder, mental retardation, a history of severe somatisation or psychotic disorders, or a current drug treatment that might modify either gastrointestinal function or the 5-HT system (analgesic medication, anxiolytics, or antidepressants) were excluded.

All the patients provided written informed consent after a full explanation of the protocol design which has been approved by the Institutional Review Board of the Province of Messina, Italy [Prot. N. 15/16 – 22/03/2016]; the study was conducted according to the Declaration of Helsinki.

Instruments

All the patients underwent the following battery of tools:

· Hamilton Rating Scale for Depression – HRSD (Hamilton, 1960) – Italian version (Cassano, Conti, & Levine, 1991): a 17-item semi-structured interview that assesses depressive symptoms such as depressed mood, health concerns, loss of interests, insomnia or psychomotor retardation. The items are rated on either a 3-point (0–2) or 5-point (0–4) Likert scale resulting in total scores ranging from 0 to 50. Scores ranging from 0 to 7 suggest no or minimal symptoms of depression, 8-17 indicate mild depression, 18-25 suggest moderate depression, and scores of 26 and above are associated with severe depression.

· Hamilton Rating Scale for Anxiety – HRSA (Hamilton, 1959) - Italian translation (Conti, 1999): consists of 14 items, each defined by a series of symptoms such as anxiety, tension, depressed mood, palpitations, breathing difficulties, sleep disturbances, restlessness, and other physical symptoms. This is a widely used scale and an accepted outcome measure in clinical trials. Each item is rated on a 5-point scale, ranging from 0 (not present) to 4 (severe), with a total score range of 0–56, where <17 indicates mild severity, 18–24 mild to moderate severity and 25–30 moderate to severe.

· State - Trait Anger Expression Inventory-2, STAXI-2 (Spielberger, 1999) - Italian version (Comunian, 2004): a 57-item self-report inventory which uses 4-point Likert scales to measure the intensity of anger as an emotional state (state anger; SANG), how the individual is disposed to angry feelings as a personality trait (trait anger; TANG), anger expression outward (AX-O) and inward (AX-I), anger control outward (AC-O) and inward (AC-I), and anger expression index (AX). Raw scores on STAXI-2 scales are converted to sex- and age-specific T-scores and percentile scores established in the initial validation of the scale. T-scores above 60 and below 40 are considered to fall outside the normative range.

Statistical analysis

Descriptive statistics were used to summarize the data obtained from the study. Differences among groups were assessed using the one-way analysis of variance

(ANOVA) with Bonferroni post hoc comparisons, or the χ^2-test if requested. Taking into account that multiple correlations increase the risk of Type 1 errors, a Bonferroni correction was applied, and a significance value of $p < .004$ was chosen.

Results

Out of 148 eligible patients, 111 subjects (IBS-D=37; IBS-C=34; IBS-M=40), 48 males and 63 females, were included in the study, according to inclusion and exclusion criteria. Clinical-demographic features of the study participants were reported in Table 1: no statistically significant differences among groups were observed.

Tab.1 – Clinical-demographic features of the study participants.

	IBS-D	IBS-C	IBS-M	p
Patients entered	37	34	40	-
Age (years), mean ± SD	46.7±11.7	47.6±10.1	45.6±13.9	.937 [a]
Sex (M/F)	15/22	16/18	17/23	.852 [b]
Duration of illness (months), mean ± SD	31.7±32.3	29.3±34.6	33.8±48.8	.968 [a]

[a] ANOVA; b χ^2-test

Table 2 shows statistical analyses of the psychometric instruments applied in study participants. According to mean HRSD scores, the severity of depressive symptoms was “moderate” in IBS-C patients and “mild” in IBS-D and IBS-M patients (17.15±6.7 vs 14.24±6.6 vs 12.50±4.9); nevertheless, no statistically significant differences were documented among IBS subtypes.

Severity of anxiety symptoms, as assessed by HRSA, was “mild to moderate” in IBS-C patients (mean = 18.53 ± 7.7), and “mild” in IBS-D (mean = 13.35 ± 7.1) and IBS-M (mean = 13.25 ± 4.7) patients; statistically significant differences among subgroups were found (Bonferroni Post-hoc test- IBS-C vs IBS-D: p=0.004; IBS-C vs IBS-M: p=0.003).

Regarding STAXI-2 questionnaire, mean scales and subscales scores were within the normal range for all groups. Nevertheless, there was a trend in IBS-C to have higher scores than those of IBS-D and IBS-M groups on almost all STAXI-2 scales and subscales; the few exceptions to this trend concerned the subscales AC-O and AC-I, whose mean scores were lower than the two other groups’ scores. Statistically significant differences among subgroups emerged only at SANGF and AX-I variables, both higher in IBS-C group than in IBS-M group (Bonferroni Post-hoc test- SANGF: IBS-C vs IBS-M: p=0.002; AX-I: IBS-C vs IBS-M: p=0.001).

Tab.2 – HRSD, HRSA and STAXI 2 mean scores in study participants.

	IBS-D (n=37)		IBS-C (n=34)		IBS-M (n=40)		ANOVA	
	Mean	SD	Mean	SD	Mean	SD	F	p
HRSD	14.24	6.6	17.15	6.7	12.50	4.9	5.341	.006
HRS-A	13.35	7.1	18.53	7.7	13.25	4.7	7.422	.001
SANG	45.30	3.8	50.24	12.6	45.05	2.9	5.304	.006

SANGF	46.65	5.7	50.88	10.4	45.30	3.1	6.319	.003
SANGV	44.65	6.6	49.18	10.1	46.05	4.6	3.471	.035
SANGP	45.35	1.8	49.65	13.4	45.00	1.1	4.197	.018
TANG	48.38	6.9	52.35	11.9	50.65	12.5	1.212	.302
TANGT	48.32	7.1	51.24	14.1	48.90	10.3	.724	.487
TANGR	49.14	10.5	53.24	11.2	50.25	13.3	1.121	.330
AX-O	47.73	12.1	50.91	11.5	48.60	9.4	.764	.468
AX-I	49.68	10.1	54.35	8.8	46.00	9.7	6.911	.001
AC-O	49.60	9.2	47.59	10.7	51.70	8.9	1.674	.192
AC-I	51.37	9.5	50.65	10.5	52.15	10.9	.193	.825
AX	49.78	9.9	51.82	10.1	45.65	10.3	3.600	.031

HRSD = Hamilton Depression Rating Scale; HRSA = Hamilton Rating Scale for Anxiety; SANG = State Anger; SANGF = State Anger / Feeling Angry; SANGV = State Anger / Feel like Expressing Anger Verbally; SANGP = State Anger / Feel like Expressing Anger Physically; TANG = Trait Anger; TANGT = Trait Anger / Angry Temperament; TANGR = Trait Anger / Angry Reaction; AX-O = Anger Expression-Out; AX-I = Anger Expression-In; AC-O = Anger Control-Out; AC-I = Anger Control-In; AX = Anger Expression index.

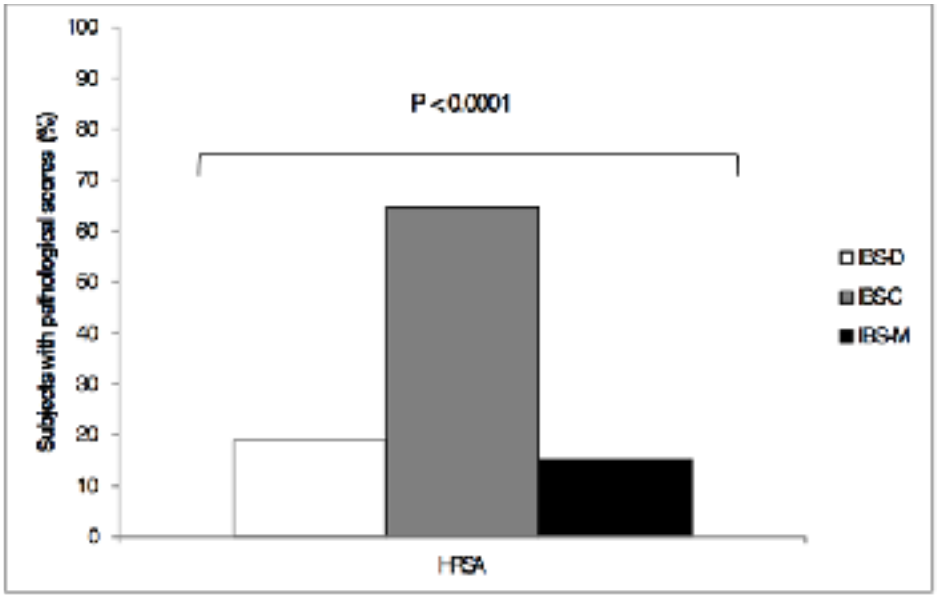
Regarding the frequencies (expressed in percentages) of subjects who reported scores in the clinical range within the three subtypes (Table 3), statistically significant differences among subgroups emerged only at HRSA variable ($\chi 2=25.122$; $p<.0001$), with twenty-two subjects (64.7%) from the IBS-C group showing pathological scores at this subscale (Fig. 1).

	IBS-D (n=37)		IBS-C (n=34)		IBS-M (n=40)		Chi – square test (df=2)	
	n	%	n	%	n	%	X^2	p
HRSD	32	86.5	30	88.2	35	87.5	.050	.975
HRSA	7	18.9	22	64.7	6	15	25.122	<.0001
SANG	1	2.7	3	8.8	0	0	4.249	.120
SANG F	3	8.1	3	8.8	0	0	3.591	.166
SANG V	1	2.7	4	11.8	0	0	6.332	.042
SANG P	0	0	3	8.8	0	0	6.983	.030
TANG	2	5.4	10	29.4	11	27.5	7.966	.019
TANG T	2	5.4	5	14.7	3	7.5	2.043	.360
TANG R	7	18.9	11	32.4	14	35	2.719	.257
AX-O	4	10.8	6	17.6	3	7.5	1.874	.392
AX-I	8	21.6	10	29.4	5	12.5	3.227	.199
AC-O	7	18.9	5	14.7	6	15	.300	.861
AC-I	11	29.7	10	29.4	14	35	.349	.840
AX	7	18.9	6	17.6	3	7.5	2.447	.294

Table 3. Frequencies of subjects with pathological scores on HRSD, HRSA and STAXI 2.

HRSD = Hamilton Depression Rating Scale; HRSA = Hamilton Rating Scale for Anxiety; SANG = State Anger; SANGF = State Anger / Feeling Angry; SANGV = State Anger / Feel like Expressing Anger Verbally; SANGP = State Anger / Feel like Expressing Anger Physically; TANG = Trait Anger; TANGT = Trait Anger / Angry Temperament; TANGR = Trait Anger / Angry Reaction; AX-O = Anger Expression-Out; AX-I = Anger Expression-In; AC-O = Anger Control-Out; AC-I = Anger Control-In; AX = Anger Expression index.

Fig. 1 - Frequencies of subjects who reported pathological scores in the Hamilton Rating Scale for Anxiety (HRSA)



Discussion

Our results showed that IBS-C patients were characterized by higher levels of anxiety than the other two subgroups. Moreover, analyzing the frequencies, a consistent number of subjects (64.7%) from the IBS-C subgroup had anxiety scores within the pathological range. Furthermore, although not statistically significant, differences in depression were also found, with IBS-C patients showing a trend to experience more depressive symptoms than IBS-D and IBS-M patients.

The current findings are in keeping with previous studies that documented higher levels of emotional distress, anxiety and/or depression in IBS-C subtype (Cho et al., 2011; Eriksson, Andrén, Eriksson, & Kurlberg, 2008; Muscatello et al., 2010; Rey de Castro et al., 2015). Contrarily, other studies have identified IBS-D (Guthrie et al., 2003; Singh et al., 2015; Sugaya, Kaiya, Kumano, & Nomura, 2008) and, to a lesser extent, IBS-M (de Medeiros et al., 2008) as the more psychologically distressed subtypes, considering also disease-specific quality of life measures (Singh et al., 2015), and cognitive appraisal of IBS symptoms (Sugaya et al., 2008). Differences in methodology, sampling, recruitment (i.e.: internet- or telephone-based interviews), study design (i.e.: retrospective), definition of negative emotions and/or emotional distress may partially explain the conflicting data emerged from this research area. Another possible source of discrepancies is that most studies used the Hospital Anxiety Depression Scale (HADS) (Zigmond & Snaith, 1983), a 14-item measure designed to be used as a brief screen for depression (seven items) and anxiety (seven items). The HADS is considered the first step in a multistage process of selecting individuals at risk to be evaluated through further, more accurate questionnaires and/or clinical interviews, since it does not assess neither symptom severity and frequency, nor specific, nuclear mood and anxiety features (i.e.: low mood, chronic worry, and guilt).

Regarding anger, although no statistically significant differences were found, IBS-C subjects scored higher than D-IBS subjects at all STAXI-2 scales, except for the two scales measuring anger control oriented outward or inward, whose scores were lower in IBS-C patients when compared with IBS-D subjects. These trends confirm our previous findings on the tendencies, by IBS-C subjects, to experience angrier feelings, along with reduced abilities to effectively control anger expression than IBS-D subgroup (Muscatello et al., 2010). Moreover, IBS-C patients scored significantly higher than IBS-M subjects on the SANGF subscale (reflects the intensity of a variety of angry feelings), and on the AX-I scale (tendency to suppress angry feelings inward). Suppression of negative emotions is viewed as a maladaptive regulation strategy (Gross & John, 2003) with negative consequences for health and well-being; particularly, anger suppression

has been related to a number of mental and somatic illnesses, including gastrointestinal disorders and IBS (Beesley, Rhodes, & Salmon, 2010; Bennet, Evans, Dowsett, & Kellow, 2009; Welgan, Meshkinpour, & Ma, 2000).

It is difficult to compare our findings with the available literature, since few studies have examined possible association between anger and IBS (Beesley et al., 2010; Bennet et al., 2000; Evans, Bennett, Bak, Tennant, & Kellow, 1996; Welgan et al., 2000; Zoccali al., 2006), and only our previous research has investigated the dimension of anger in different IBS subtypes (Muscatello et al., 2010).

According to the obtained results, it seems that IBS-C patients constitute a subgroup characterized by a discrete burden of negative emotions, mainly anxiety and anger. Anxiety and anger are linked through shared physiological reactions to stress, since individuals may react either with anger or anxiety ("fight" or "flight" response) when confronted with threats. From a clinical point of view, irritability, defined as a lowered threshold for anger, is a symptom of Generalized Anxiety Disorder, and high levels of anger, internalized anger expression, and lower anger control were found in anxious individuals (Deschênes, Dugas, Fracalanza, & Koerner, 2012). Both anxiety and anger lead to enhanced vigilance toward the external and/or internal environments for detecting potential threats; this, along with the emotional arousal, involves the activation of the sympathetic nervous system (Smith, Ruiz, & Uchino, 2000); a relative hyperfunction of the sympathetic activity concomitant with a relative hypofunction of the parasympathetic activity have been described in anxiety disorders (Brown, Chorpita, & Barlow, 1998), and in IBS, in which the increased sympathetic tone seems to enhance visceral hypersensitivity (Ng, Malcolm, Hansen, & Kellow, 2007). In addition, anxiety and anger usually share those underlying cognitive vulnerabilities frequently observed in IBS (McKinnon, Van Oudenhove, Tack, & Jones, 2015), such as catastrophizing, the attitude to put emphasis on the threat value of painful stimuli, and intolerance of uncertainty, a cognitive construct arising from the negative belief that uncertainty is unfair. Finally, anxiety and

anger are expressions of underlying constitutional or biological factors, such as a hyperresponsive nervous system (Suinn, 2001) or individual differences in serotonin (5-HT) levels. In the brain-gut-axis, altered 5-HT signaling contributes to abnormal gut function and hypersensitivity in IBS (Stasi, Bellini, Bassotti, Blandizzi, & Milani, 2014); furthermore, an impairment of 5-HT release has been shown in IBS-C subtype (Choi et al., 2014; Spiller, 2008), and it could be hypothesized that the serotonergic hypofunction may also contribute to the higher burden of negative emotions found in IBS-C subtype.

The present study presents several limitations: the small sample size may have limited its accuracy to detect differences between the groups. Then, eligible subjects were recruited from IBS patients referred from an endoscopy clinic; therefore, they are likely to be affected by a more severe form of the disorder if compared with IBS patients from primary care or general population settings. Moreover, the cross-sectional design does not allow the detection of possible switches of a subtype into another, also considering that bowel pattern subtypes can be highly unstable. Finally, the lack of an assessment of IBS symptom severity does not allow to clarify a possible effect on psychopathology of the disease severity.

Beyond the aforementioned limitations, our study highlighted stimulating relationships between IBS subtypes and negative aspects of the emotional domain and demonstrated that IBS-C subtype shows an emotional profile characterized by higher levels of anxiety and anger.

Since IBS is actually viewed as a heterogeneous and multifactorial disease, more comprehensive approach including the emotional, cognitive, and psychosocial components of the brain-gut axis may improve our knowledge on the pathophysiological and clinical aspects of the disease and may have significant implications for treatments and clinical outcome.

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