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Alexithymic characteristics and interoceptive abilities are associated with disease severity and levels of C-reactive protein and cytokines in patients with inflammatory bowel disease

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Abstract

Background Alexithymia and atypical gut-brain signaling have been linked to the pathophysiology of inflammatory bowel disease (IBD). We herein assessed IBD patients' alexithymia levels and interoceptive abilities, and detected potential correlations with psychological distress, symptom severity and disease activity, and inflammation indices.

Methods Adult IBD outpatients and healthy controls were recruited. Alexithymia was assessed using the Toronto Alexithymia Scale, interoceptive accuracy using the Heartbeat Counting Test (cardiac interoception) and the Water Load Test-II (gastric interoception), and interoceptive sensibility using the Multidimensional Assessment of Interoceptive Awareness (MAIA).

Results Forty-one patients with Crohn's disease (CD), 16 with ulcerative colitis (UC), and 50 healthy controls were included. In CD patients, the level of externally oriented thinking and total alexithymia score were correlated with disease activity (P=0.027 and P=0.047, respectively), while in UC patients difficulties in identifying emotions were linked to disease activity (P=0.007). In CD patients, the Noticing, Not-Worrying and Emotional Awareness MAIA subscale score were correlated with C-reactive protein levels (P=0.005, P=0.048 and P=0.005), the Noticing subscale score with interleukin (IL)-1β levels (r=-0.350, P=0.039), the Not-Distracting subscale score with IL-6 levels (r=-0.402, P=0.017), and the Emotional Awareness subscale score with IL-1β (r=-0.367, P=0.030) and IL-6 (r=-0.379, P=0.025) levels. Finally, in UC patients, the Not-Worrying subscale score was significantly associated with IL-6 levels (r=-0.532, P=0.049), while difficulties in identifying emotions were linked to IL-8 levels (r=0.604, P=0.022).

Conclusion Emotional and interoceptive processing is associated with IBD disease activity, suggesting a potential implication for IBD pathophysiology.

Keywords Alexithymia, cytokines, inflammatory bowel disease, interoception

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Conflictof Interest: None

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Introduction

Patients with inflammatory bowel disease (IBD) appear particularly vulnerable to the emergence of anxiety and depressive symptoms [1], and there is a bidirectional relationship between psychological distress and gastrointestinal symptoms. Research has recently focused on the complex interaction between gut-located inflammatory processes and built-in neurophysiological mechanisms underlying specific patterns of emotional and physiological reactivity that might confer increased disease risk. Emotional processing difficulties—described by the term alexithymia, which reflects deficits in the perception and expression of emotions—have

been extensively studied in psychiatric and psychosomatic patients, including IBD patients [2]. Alexithymic traits are quite prevalent in a subgroup of IBD patients who also report increased psychiatric comorbidity, greater everyday suffering and a poorer prognosis [3]. In addition, it has been proposed that alexithymia as a stable personality characteristic reflects a potential genetic predisposition to stress-mediated somatization and disturbed autoimmunity, which may eventually lead to physical and psychological morbidity [2].

Alexithymia has also been linked to disturbed interoceptive abilities, mainly impairment in the subjective awareness of interoception [4]. Interoception refers to the ability to detect and process internal bodily sensations and is directly linked to the processing of emotional stimuli [5]. IBD patients report a different pattern of interoceptive sensibility, namely increased emotional awareness and a greater tendency to distract themselves from unpleasant sensations compared to healthy controls [6]. In addition, patients with chronic gastrointestinal disorders, including IBD, present altered neural processing of pain stimuli [7] and report higher levels of visceral hypersensitivity [8]. In this context, the aim of the present case-control study was the evaluation of IBD patients' alexithymia levels and interoceptive abilities, and the detection of potential correlations of these parameters with psychological distress, body image, symptom severity and disease activity, and inflammation indices. To our knowledge, this is the first study that assesses multiple dimensions of alexithymia and interoception using well-validated psychometric instruments in IBD patients, and attempts to link them not only to psychosocial functioning, but also to the underlying chronic inflammation processes.

Patients and methods

The present case–control cross-sectional study was conducted in the Gastroenterology Division of the University Hospital of Patras (UHP), Greece, with the collaboration of the Psychiatry Department. The study protocol was approved by the hospital's Ethics Committee (File No: 922/25/10/2018). All study participants provided written informed consent prior to study enrolment.

Adult IBD outpatients and healthy controls recruited from the community were invited to enter the study between November 2019 and May 2020. The following exclusion criteria were used: illicit drug use or alcohol abuse during the last year, stroke, cancer, cerebrovascular disease, mental retardation, dementia, psychotic or bipolar disorder, mindfulness-based therapy and lack of fluency in the Greek language. All healthy controls provided access to their electronic medical charts, which were thoroughly screened for disease and medication history. In addition, they were interviewed regarding the presence of current psychiatric or gastrointestinal symptoms to exclude cases of psychiatric or gastrointestinal disease.

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Psychometric instruments and tests

Psychological functioning was assessed using the Greek version of the Hospital Anxiety and Depression Scale (HADS) [9], which comprises 7 items for anxiety and 7 items for depression. Each subscale is scored from 0-21. Higher scores indicate greater symptom severity [10].

Body image was assessed using the Modified Body Image Scale [11]. This is a 9-item self-administered questionnaire originating from the Body Image Scale, which evaluates body image in cancer patients [12] and has been validated in the Greek language [13]. The modified scale has been used previously in IBD patients, showing satisfactory psychometric properties. Each item is scored from 0 (not at all) to 3 (very much) and higher scores indicate increasing body image dissatisfaction [11,12].

Symptom severity was assessed with a set of items regarding the presence of 7 symptoms frequently reported by IBD patients (nausea, vomiting, abdominal pain, diarrhea, bloating, constipation, incontinence) and the impairment caused by each symptom during the last week. The presence of symptoms was detected with a yes/no question and the degree of impairment was defined at 3 levels: not at all, a little, or a lot. Prior to questionnaire completion, all participants were instructed regarding the definition of each gastrointestinal symptom.

Alexithymia was measured with the Greek version of the Toronto Alexithymia Scale [14]. This is a 20-item instrument and each item is scored on a 5-point scale ranging from 1=strongly disagree to 5=strongly agree. It encompasses 3 subscales, 1 that measures difficulties in identifying feelings and distinguishing them from bodily sensations, 1 that assesses deficits in describing feelings, and 1 that measures externally oriented thinking. Higher scores indicate more difficulties. Additionally, a total alexithymia score is calculated from all items [15].

Interoception is a multidimensional construct comprising 3 distinct processes: interoceptive accuracy, interoceptive sensibility and interoceptive awareness. Interoceptive accuracy is the ability to detect and track internal bodily sensations, which can be measured by objective performance tests. Interoceptive sensibility refers to the subjective belief regarding one's interoceptive abilities and the degree of one's engagement with interoceptive signals; it is evaluated using self-administered questionnaires. Interoceptive awareness is the metacognitive awareness of interoceptive abilities and is reflected by the correspondence between objective interoceptive accuracy and subjective report [16].

In the current study we evaluated cardiac and gastric interoceptive accuracy using 2 validated measures, the Heartbeat Counting Task and the Waterload Test. During the Heartbeat Counting Task, participants sat in a quiet room at a relaxing

position and were instructed to silently count their heartbeats by concentrating on their body during 3 signaled time intervals (25 sec, 35 sec, and 45 sec), which were presented in random order alternating with 60-sec periods of rest. The reported number of heartbeats was compared to the actual number of heartbeats taken by a pulse oximeter attached to the participant's index finger during the test. This procedure was repeated for a second time, and finally a total interoception score was calculated based on the IAcc formula proposed by Schandry (1981). Higher scores indicate greater interoceptive accuracy [17].

For the Waterload Test, participants were asked not to drink anything for 2 h prior to the experiment. During the test, they were asked to drink non-carbonated water at room temperature over 2 successive 5-min periods. During the first phase, participants were instructed to drink water until reaching satiation, i.e., the sensation that one has drunk enough but not too much. During the second phase, participants were asked to drink again until reaching maximum stomach fullness. During this 2-phase drink test, 3 different WLT-II indices are calculated: 1) water volume (mL) required to produce satiation (sat_ml); 2) additional water volume needed to produce maximum fullness (Δfull_ml); and 3) total water volume (total_ml), which is the sum of sat_ml and Δfull_ml [18].

Interoceptive sensibility was evaluated using the Multidimensional Assessment of Interoceptive Awareness (MAIA) which has been linguistically adapted and psychometrically validated by our research group [19]. It is a 32-item self-reported questionnaire consisting of 8 subscales: (1) the Noticing subscale, which reflects awareness of uncomfortable, comfortable, and neutral body sensations; (2) the Not-Distracting subscale, which reflects the tendency not to ignore or distract oneself from sensations of pain or discomfort; (3) the Not-Worrying subscale, which reflects the tendency not to worry or experience emotional distress with sensations of pain or discomfort; (4) the Attention Regulation subscale, which represents the ability to sustain and control attention to body sensations; (5) the Emotional Awareness subscale, which refers to awareness of the connection between body sensations and emotional states; (6) the Self-Regulation subscale, which reflects the ability to regulate distress by attention to body sensations; (7) the Body-Listening subscale, which refers to actively listening to the body for insight; and (8) the Trusting subscale, which refers to the experience of one's body as safe and trustworthy. MAIA items are rated on a 6-point Likert Scale (0-5), and higher scores indicate greater interoceptive sensibility [20].

All participants provided demographic data. For the IBD group, clinical and laboratory data were extracted from their medical records to calculate disease activity indices, the Truelove-Witts Index for ulcerative colitis (UC) [21] and the Harvey-Bradshaw Index for Crohn's disease (CD) [22].

Measurement of serum cytokine levels

Blood samples were drawn from patients to measure serum concentrations of cytokines interleukin (IL)-8, IL-1β, IL-6, IL-10, tumor necrosis factor-α, and IL-12p70, by flow cytometry using a cytometric bead array assay (BD™ CBA Human Inflammatory Cytokines Kit 551811). The serum was separated from blood after clotting at room temperature within 1 h by centrifugation (1500 g for 10 min). Serum was aliquoted and stored at -80°C until analysis.

Statistical analysis

Statistical analysis was performed using the SPSS package (version 17.0 for Windows; SPSS Inc., Chicago, Illinois, USA). The sample size was calculated with the formula used for case-control studies [23]. Numerical data were expressed as medians and interquartile ranges, and categorical data as counts and percentages. All variables were tested for normal distribution using the Shapiro-Wilk test. Between-group differences in alexithymia, interoception, psychological distress, body image and gastrointestinal (GI) symptom severity were assessed by the chi-squared test for categorical variables, and the Kruskal-Wallis test for continuous variables. Subsequently, we used Spearman's correlations (continuous variables) and Mann-Whitney *U* or Kruskal-Wallis tests (categorical variables) to assess correlations between alexithymia and interoception and the remaining parameters separately for each group of participants. Absolute values of the correlation coefficient, r, of 0.7-1 indicate a very strong correlation, 0.5-0.7 a strong correlation, 0.3-0.5 a moderate correlation and <0.3 a weak correlation. All tests were 2-tailed and significance was set at $P<0.05$.

Results

According to the sample size calculation, a sample of 50 patients and 50 healthy controls would provide enough power to our analysis. Taking into account a potential dropout rate of 15-20%, we initially approached 120 individuals to participate, 60 IBD patients and 60 healthy controls. During recruitment, 57 patients from the IBD group consented to participate, while 50 healthy controls finally entered the study, given that 10 individuals withdrew due to the COVID-19 lockdown measures imposed on March 11, 2020. Thus, in total, 107 participants were enrolled, 41 CD patients, 16 UC patients and 50 healthy controls. The participants' characteristics are presented in Table 1.

Psychological distress, body image, symptom severity, alexithymia and interoceptive abilities in IBD patients

Both CD and UC patients reported significantly greater anxiety (P=0.032 and P=0.008), depression (P=0.003 and P=0.008), nausea (P=0.035 and P=0.007), diarrhea (P<0.001 and P=0.011), and diarrhea-associated impairment (P<0.001 and P=0.011) compared to controls. CD patients reported a more frequent presence of abdominal pain (P=0.003), while

Table 1 Participants' demographic, clinical and laboratory characteristics

Characteristics	CD patients	UC patients	Healthy controls	P-value for comparisons		
				CD vs. UC	CD vs. controls	UC vs. controls
N	41	16	50			
Male sex, N (%)	26 (63.2)	6 (37.5)	26 (52.0)	0.076	0.274	0.312
Disease activity Remission or mild CD, N (%) Mild UC, N (%)	24 (70.6)	7 (58.3)				
Age, median (IQR), y	39.0 (28.0-48.0)	40.0 (25.8-43.8)	38.0 (31.0-49.25)	0.594	0.848	0.423
Education, median (IQR), y	16.0 (12.0-16.0)	16.0 (12.0-16.0)	16.0 (12.0-16.0)	0.709	0.287	0.649
Family status, N (%) Single Married without children Married with children Divorced, widow(er)	 13 (33.3) 1 (2.3) 22 (56.4) 3 (7.7)	 8 (56.2) 1 (6.7) 6 (40.0) 0 (0.0)	 19 (38.8) 4 (8.2) 22 (44.9) 4 (8.2)	0.344	0.581	0.594
Hgb (g/dL), median (IQR)	14.1 (12.9-15.1)	14.3 (12.8-15.2)	-	0.726	-	-
WBC, median (IQR)	8055 (6578-9473)	7060 (6230-10400)	-	0.608	-	-
PLT, median (IQR)	267500 (222750-351750)	298000 (242000-358000)	-	0.265	-	-
PT (sec), median (IQR)	13.5 (13.1-15.05)	13.2 (12.65-14.05)	-	0.064	-	-
Albumin (g/dL), median (IQR)	4.4 (3.9-4.60)	4.4 (4.2-4.6)	-	0.741	-	-
CRP (mg/dL), median (IQR)	0.35 (0.22-0.89)	0.43 (0.22-0.79)	-	0.889	-	-
ESR (mm/h), median (IQR)	12.5 (5.0-24.3)	12.5 (4.8-17.5)	-	0.602	-	-

CD, Crohn's disease; UC, ulcerative colitis; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Hgb, hemoglobin; WBC, white blood count; PLT, platelets; PT, prothrombin time

UC patients reported a more frequent presence of incontinence (P=0.041) and increased body image disturbance (P<0.001), compared to healthy controls. Between-group comparisons of psychological distress, body image, and GI symptom frequency and severity are depicted in Supplementary Table 1.

Both CD and UC patients presented a higher total alexithymia score (P=0.044 and P=0.036 respectively), compared to healthy controls, while CD patients reported greater difficulties in describing feelings (P=0.027). UC patients exhibited higher cardiac interoceptive accuracy and lower body trusting, compared to CD patients (P=0.021 and P=0.013) and healthy controls (P=0.006 and P=0.001). CD patients reported gastric satiety at a significantly lower water volume (P<0.001) compared to healthy controls. However, both patient groups reported maximum fullness at significantly lower water volumes compared to the control group (P<0.001 and P=0.003). Between-group comparisons of alexithymia, cardiac and gastric interoception scores are presented in Table 2.

Correlations between alexithymia traits, symptom severity, body image and psychological distress in IBD patients and healthy controls (Supplementary Table 2)

In CD patients, difficulties in identifying feelings were strongly correlated with body image disturbances (r=0.570, P<0.001), nausea (P=0.015), and abdominal pain (P=0.031). Difficulties in describing feelings were linked to body image disturbances (r=0.350, P=0.029) and incontinence (P=0.049), while total alexithymia score was significantly correlated with body image disturbances (r=0.428, P=0.007), and nausea (P=0.045). In UC patients, difficulties in identifying feelings were associated with the degree of abdominal pain-induced impairment (P=0.042), externally oriented thinking was negatively correlated with body image disturbances (r=-0.521, P=0.038), and total alexithymia score was strongly associated with incontinence (P=0.020). Given that alexithymia scores did not correlate with anxiety and depression scores in IBD patients, we performed a similar correlation analysis between alexithymia scores and HADS scores in the healthy control group. Difficulties in identifying feelings were strongly correlated with anxiety (r=0.463, P=0.001) and depression (r=0.400, P=0.005) scores; difficulties in describing feelings were associated with anxiety (r=0.345, P=0.017) and depression (r=0.364, P=0.012) scores; and the total alexithymia score was significantly correlated with anxiety (r=0.318, P=0.029) and depression scores (r=0.340, P=0.019) in healthy individuals.

Correlations between alexithymic traits, disease activity and laboratory indices in IBD patients

The Harvey-Bradshaw Index was used to classify CD patients in being in clinical remission or not, while the

Table 2 Between group comparisons of scores for alexithymia and interoceptive abilities

Scores	CD patients	UC patients	Healthy controls	P-value for comparisons		
				CD vs. UC	CD vs. controls	UC vs. controls
DIF, median (IQR)	18.0 (11.0-24.0)	16.0 (12.25-24.25)	13.0 (9.5-18.0)	0.913	0.091	0.104
DDF, median (IQR)	14.0 (10.0-17.0)	14.0 (9.25-18.5)	11.0 (7.25-15.0)	0.956	0.027	0.066
EOT, median (IQR)	20.0 (16.0-24.0)	22.0 (18.25-23.0)	20.0 (15.0-22.0)	0.467	0.569	0.195
TAS total, median (IQR)	52.0 (40.5-61.0)	49.0 (45.0-61.75)	44.0 (36.0-55.75)	0.765	0.044	0.036
Cardiac interoception score, median (IQR)	0.28 (0.0-0.71)	0.69 (0.37-0.82)	0.29 (0.0-0.57)	0.021	0.634	0.006
Water satiety volume, median (IQR)	155.0 (118.8-250.0)	250.0 (140.0-297.5)	255 (200.0-500.0)	0.148	<0.001	0.152
Water discomfort volume, median (IQR)	385.0 (207.5-500.0)	420.0 (235.0-518.75)	620.0 (470.0-950.0)	0.864	<0.001	0.003
Total water volume, median (IQR)	565. (340.0-750.0)	640.0 (556.25-765.0)	880.0 (680.0-1400.0)	0.481	<0.001	0.009
MAIA noticing, median (IQR)	3.0 (1.75-3.9)	3.25 (1.94-3.94)	3.75 (2.75-4.25)	0.792	0.066	0.120
MAIA not distracting, median (IQR)	1.67 (1.0-2.33)	2.0 (1.08-2.92)	1.67 (1.0-2.33)	0.320	0.928	0.320
MAIA not worrying, median (IQR)	2.33 (1.67-3.0)	2.33 (1.42-3.67)	2.5 (1.92-3.42)	0.935	0.504	0.578
MAIA attention regulation, median (IQR)	3.0 (2.07-3.68)	2.64 (1.46-3.29)	3.29 (2.36-3.75)	0.123	0.730	0.101
MAIA emotional awareness, median (IQR)	3.7 (2.85-4.55)	3.3 (2.05-4.3)	3.6 (2.0-4.4)	0.191	0.377	0.486
MAIA self-regulation, median (IQR)	2.63 (1.75-3.5)	2.13 (0.81-3.38)	2.75 (1.69-3.75)	0.268	0.919	0.330
MAIA body listening, median (IQR)	2.33 (1.67-2.92)	2.33 (1.17-3.58)	2.67 (1.33-3.33)	0.956	0.614	0.860
MAIA trusting, median (IQR)	4.0 (3.3-4.67)	2.67 (2.33-3.67)	4.0 (3.67-4.67)	0.013	0.421	0.001

IQR, interquartile range; MAIA, multidimensional assessment of interoceptive awareness; DIF, difficulty identifying feelings subscale; DDF, difficulty describing feelings subscale; EOT, externally oriented thinking subscale; TAS, Toronto alexithymia scale; CD, Crohn's disease; UC, ulcerative colitis

Truelove-Witts was used to classify UC patients as suffering from mild or moderate disease. In CD patients, more externally oriented thinking and a higher total alexithymia score correlated with the presence of active disease (P=0.027 and P=0.047, respectively). In UC patients, difficulties in identifying feelings were linked to the presence of moderate disease activity (P=0.007) (Table 3).

Correlations between interoception accuracy scores, alexithymia, psychological distress, body image, GI symptom severity and disease activity in IBD patients (Supplementary Tables 3, 4)

In CD patients, cardiac interoceptive accuracy was negatively correlated with externally oriented thinking (r=-0.443, P=0.04) and total alexithymia score (r=-0.313, P=0.049), while a smaller water volume to satiety (high gastric interoceptive accuracy) was associated with bloating (P=0.029) and the degree of bloating-associated impairment (P=0.047), while a smaller water volume to fullness (high gastric interoceptive accuracy) was significantly linked to incontinence (P=0.031). In UC patients, increased cardiac interoceptive accuracy was linked to abdominal pain (P=0.049) and constipation (P=0.021), while higher gastric interoceptive accuracy (smaller water volume to satiety) was strongly correlated with difficulties in describing feelings (r=-0.590, P=0.016) and total alexithymia score (r=-0.613, P=0.011). In this patient group, constipation was also linked to lower gastric interoceptive accuracy (higher water volume to satiety, P=0.011 and greater total water volume, P=0.048).

Correlations between interoceptive sensibility scores and anxiety, depression, body image, alexithymia, GI symptom severity and disease activity in IBD patients (Supplementary Tables 5-7)

In CD patients, the Noticing score was significantly correlated with anxiety (r=0.549, P=0.001), depression (r=0.356, P=0.042), body image disturbances (r=0.356, P=0.026), abdominal pain (P=0.024), and C-reactive protein (CRP) levels (P=0.005). The Not-Worrying score was significantly correlated with anxiety (r=-0.407, P=0.019), body image disturbances (r=-0.405, P=0.010), difficulties in identifying (r=-0.349, P=0.027) and describing feelings (r=-0.368, P=0.016), total alexithymia score (r=-0.342, P=0.031), nausea (P=0.018), abdominal pain (P=0.003), gas and bloating (P=0.049), and CRP levels

Table 3 Correlations between alexithymia traits, disease activity indices and laboratory indices in patients with inflammatory bowel disease

Laboratory indices	DIF		DDF		EOT		TAS TOTAL	
	CD	UC	CD	UC	CD	UC	CD	UC
Hgb (g/dL)								
r	0.227	-0.199	0.212	-0.350	-0.070	-0.052	0.165	-0.323
P-value	0.165	0.476	0.195	0.201	0.672	0.853	0.316	0.240
WBC								
r	0.138	-0.171	0.072	-0.302	-0.104	0.143	0.055	-0.217
P-value	0.415	0.543	0.671	0.274	0.538	0.612	0.747	0.437
PLT								
r	-0.109	0.038	-0.007	0.059	-0.140	-0.080	-0.100	-0.029
P-value	0.508	0.894	0.966	0.835	0.395	0.776	0.546	0.919
PT (sec)								
r	-0.022	0.090	-0.226	-0.033	0.209	0.033	-0.024	0.039
P-value	0.910	0.770	0.247	0.914	0.285	0.914	-0.905	0.900
Albumin (g/dL)								
r	-0.043	0.034	-0.046	0.199	-0.230	0.556	-0.127	0.239
P-value	0.800	0.903	0.785	0.477	0.165	0.032	0.447	0.391
CRP level, median (IQR)								
Normal	19 (11-24.5)	16.5 (12.3-24.3)	16 (9.5-18)	14 (10.3-18)	20 (16.5-24)	22 (18.3-23.8)	56 (43-62)	49.5 (45.3-61.8)
Increased	18 (9.5-24.5)	15 (11-22.8)	12 (9.5-14.5)	13 (9-19.3)	20 (15.5-24.5)	21 (17-22)	47 (37-62.5)	45.5 (45-59.5)
P-value	0.758	0.670	0.295	0.854	0.975	0.463	0.655	0.543
ESR level, median (IQR)								
Normal	12 (8.5-24)	13 (10.8-18.5)	14 (5.5-18)	12 (8-15.5)	18 (14-24)	21 (18.8-24.5)	45 (27-59.5)	46.5 (40.5-57.8)
Increased	19.5 (11-22.8)	18 (13.8-25)	13 (10-17.8)	14.5 (10.5-19.3)	20 (17.5-23.5)	22 (17.5-22.3)	52 (40.5-62.5)	49.5 (45.8-64.8)
P-value	0.389	0.210	0.714	0.249	0.231	0.584	0.408	0.157
CD disease activity (Harvey-Bradshaw Index)								
Clinical remission	12 (10-21)		11.5 (9.3-16.3)		18 (14.3-20.8)		44.5 (35.5-51.5)	
Mild to severe disease	21 (12.5-25)		14.5 (8.5-18.3)		22 (18.8-25.3)		58 (45-68.5)	
P-value	0.104		0.268		0.027		0.047	
UC disease activity (Truelove-Witts Index), median (IQR)								
Mild		13 (10-14)		14 (9-20)		19 (18-22)		46 (44-49)
Moderate		22 (17.5-25)		14 (10-20.5)		22 (16.5-26.5)		58 (47-69)
P-value		0.007*		0.743		0.461		0.072

DIF, difficulty identifying feelings subscale; DDF, difficulty describing feelings subscale; EOT, externally oriented thinking subscale; TAS, Toronto alexithymia scale; CD, Crohn's disease; UC, ulcerative colitis; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Hgb, hemoglobin; WBC, white blood count; PLT, platelets; PT, prothrombin time; IQR, interquartile range

(P=0.048). The Attention Regulation score was associated with difficulties in identifying (r=-0.395, P=0.012) and describing feelings (r=0.324, P=0.042), total alexithymia score (r=-0.327, P=0.039) and the degree of diarrhea-associated impairment (P=0.029). The Emotional Awareness score was linked to anxiety (r=0.452, P=0.008), nausea (P=0.047), and CRP levels (P=0.005). Finally, the Trusting score was strongly correlated with anxiety (r=-0.448, P=0.010), body image disturbances (r=-0.419, P=0.009), difficulties in identifying (r=-0.368, P=0.021) and describing (r=-0.355, P=0.027) feelings, and nausea (P=0.018).

In UC patients, the Noticing score was associated with the degree of diarrhea-associated impairment (P=0.025), and with gas and bloating (P=0.030). The Not-Distracting score was strongly correlated with abdominal pain (P=0.020) and the degree of its associated impairment, (P=0.042), and with gas and bloating (P=0.042) and the degree of its associated impairment (P=0.039). The Attention Regulation score was linked to constipation (P=0.037), while the Emotional Awareness score was correlated with body image disturbances (r=0.516, P=0.041) and the degree of diarrhea-associated impairment (P=0.029). The Self-Regulation and the Body Listening scores were also significantly associated with the degree of diarrhea-associated impairment (P=0.016 and P=0.029, respectively). Finally, the Trusting score was linked to anxiety severity (r=-0.571, P=0.021), the degree of diarrhea-associated impairment (P=0.025) and constipation (P=0.047).

Correlations between alexithymia, interoceptive processing and serum cytokines levels (Table 4)

In CD patients, the Noticing score was correlated with IL-1β levels (r=-0.350, P=0.039), the Not-Distracting score was significantly associated with IL-6 levels (r=-0.402, P=0.017) and the Emotional Awareness score was correlated with IL-1β (r=-0.367, P=0.030) and IL-6 (r=-0.379, P=0.025) levels. In UC patients, the Not-Worrying score was strongly associated with IL-6 levels (r=-0.532, P=0.049), while difficulties in identifying feelings were linked to IL-8 levels (r=0.604, P=0.022). All other correlations were non-significant. Fig. 1 summarizes all significant correlations of alexithymia and interoception with multiple variables for each patient group.

Discussion

In the present study we assessed multiple dimensions of alexithymia and interoception in IBD patients and revealed a distinct profile of emotional and internal bodily sensation processing contrasting with that of healthy individuals. Both CD and UC patients reported difficulties in describing emotions, and displayed greater gastric interoceptive accuracy, while UC patients also exhibited better cardiac interoceptive accuracy and significant differences in interoceptive sensibility. Moreover, we found significant

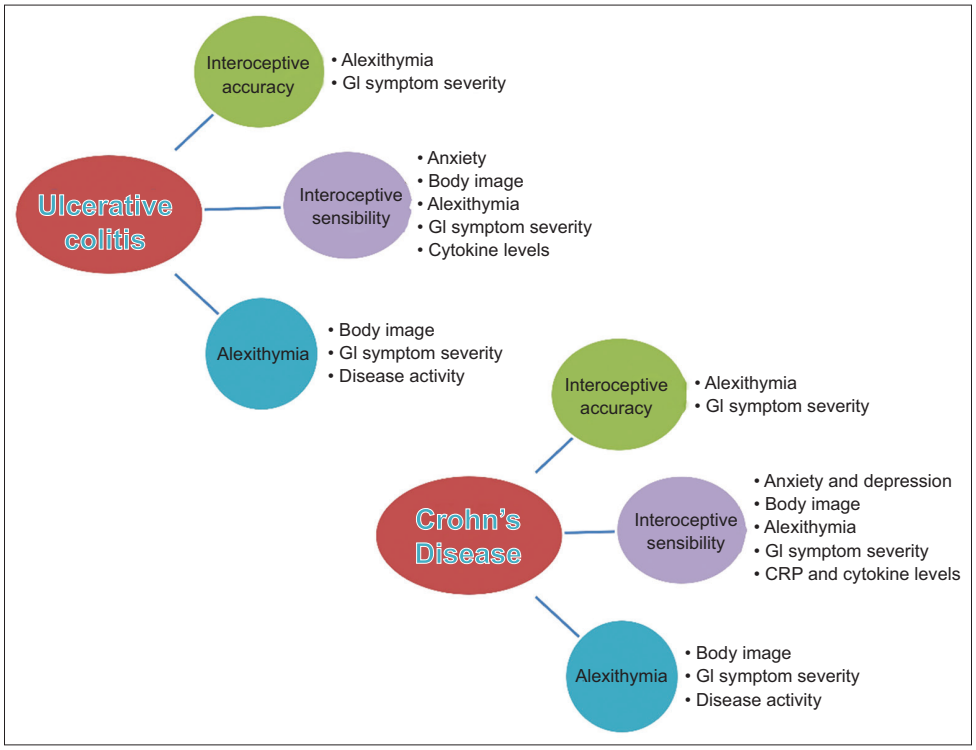

Figure 1 Significant correlations of alexithymia and interoception in patients with Crohn's disease and in those with ulcerative colitis
GI, gastrointestinal; CRP, C-reactive protein

Table 4 Correlations between alexithymia, interoceptive sensibility, interoceptive accuracy and cytokine levels by patient group

Parameters	IL-1β (pg/mL)				IL-6 (pg/mL)				IL-8 (pg/mL)				TNF (pg/mL)			
	CD		UC		CD		UC		CD		UC		CD		UC	
	r	P-value	r	P-value	r	P-value	r	P-value	r	P-value	r	P-value	r	P-value	r	P-value
DIF	-0.134	0.442	-	-	-0.031	0.861	0.139	0.635	-0.071	0.683	0.604	0.022	-0.016	0.928	-	-
DDF	0.021	0.907	-	-	0.036	0.837	-0.212	0.466	-0.053	0.762	0.228	0.432	-0.082	0.639	-	-
EOT	-0.139	0.427	-	-	-0.187	0.283	0.089	0.762	-0.136	0.437	-0.188	0.688	-0.010	0.954	-	-
Interoception score	<0.001	0.998	-	-	0.252	0.144	-0.027	0.926	0.080	0.648	0.229	0.431	-0.037	0.835	-	-
Water satiety volume	0.056	0.775	-	-	0.004	0.983	0.021	0.944	-0.027	0.890	-0.337	0.239	0.142	0.462	-	-
Water discomfort volume	0.224	0.253	-	-	-0.093	0.638	0.359	0.207	-0.076	0.701	0.182	0.533	0.043	0.828	-	-
Total water volume	0.137	0.488	-	-	-0.048	0.809	0.310	0.280	-0.023	0.908	-0.029	0.923	0.068	0.730	-	-
MAIA noticing	-0.350	0.039	-	-	-0.127	0.465	0.233	0.422	0.210	0.225	0.049	0.869	0.155	0.373	-	-
MAIA not distracting	0.059	0.738	-	-	-0.402	0.017	-0.046	0.876	-0.280	0.103	-0.163	0.577	-0.057	0.746	-	-
MAIA not worrying	0.244	0.159	-	-	0.301	0.079	-0.532	0.049	-0.045	0.799	0.018	0.952	-0.031	0.862	-	-
MAIA attention regulation	-0.310	0.070	-	-	-0.095	0.588	-0.033	0.910	0.100	0.567	0.131	0.656	0.235	0.175	-	-
MAIA emotional awareness	-0.367	0.030	-	-	-0.379	0.025	0.074	0.803	-0.173	0.320	0.188	0.520	0.091	0.602	-	-
MAIA self-regulation	-0.107	0.540	-	-	-0.133	0.147	-0.071	0.809	0.007	0.968	-0.130	0.658	0.251	0.146	-	-
MAIA body listening	-0.020	0.908	-	-	-0.062	0.723	-0.038	0.898	0.019	0.916	0.325	0.258	0.030	0.862	-	-
MAIA trusting	0.029	0.871	-	-	0.067	0.707	-0.269	0.353	-0.163	0.356	-0.120	0.684	-0.085	0.632	-	-

DIF, difficulty identifying feelings MAIA subscale; DDF, difficulty describing feelings MAIA subscale; EOT, externally oriented thinking MAIA subscale; MAIA, multidimensional assessment of interoceptive awareness

intercorrelations between interoceptive and emotional processing, GI symptom severity, psychological co-morbidity and inflammatory disease activity, which might imply the involvement of specific neurophysiological pathways in the pathophysiology of IBD. These findings provide valuable original knowledge and may help carve out a pathway towards novel therapeutic interventions based on the manipulation of interoceptive processing. Research has begun to focus on the effect of interoception manipulation strategies, including vagus nerve modulation and mindfulness-based therapies, on the symptomatology and course of several chronic diseases, including GI disorders [24,25].

Alexithymic traits have been repeatedly detected in IBD patients and have been linked to increased psychiatric comorbidity and greater impairment of quality of life [3,26]. In line with earlier research [3], our analysis showed similar alexithymia levels between CD and UC patients and revealed strong correlations between these difficulties and body image disturbances. Moreover, alexithymic traits were strongly correlated with disease activity and IL-8 levels, corroborating earlier findings suggesting that alexithymia is associated with changes in circulating cytokine levels [27], and that certain affective temperamental traits [28] may predispose to increased IBD activity. Given that alexithymic traits are enduring and stable temperamental characteristics, we could hypothesize that emotional processing difficulties precede disease onset, and could represent a vulnerable neurophysiological substrate that increases the likelihood of psychosomatic pathology, including the activation of neuroimmune processes that lead to the histological, endoscopic and clinical manifestations of IBD.

We found no significant association between alexithymic characteristics and psychological distress in IBD patients, a rather unexpected finding [3,29] that raises the issue of how complex is the association between alexithymia and psychological distress. Alexithymia is not a clinical disorder, but a constellation of idiosyncratic traits that raise the risk of mental or psychosomatic disease [30]. In our sample, alexithymic healthy controls displayed a high level of anxiety and depressive symptoms; alexithymic IBD patients did not, but reported a disturbed body image, increased impact of GI symptoms and greater disease severity. We could therefore hypothesize that, in IBD, emotional processing difficulties do not necessarily lead to psychological suffering, but rather manifest as somatic symptoms and a grossly altered representation of the body. Similarly, in patients with Hashimoto's thyroiditis, alexithymia score did not correlate with most dimensions of anxiety and depression symptoms, and patients with increased alexithymic traits even underreported cognitive depressive symptoms [31], suggesting that in some subpopulations of autoimmune disease patients, alexithymia predisposes individuals to the emergence of physical symptoms. Earlier research has linked alexithymic characteristics with somatosensory amplification [32] and increased vulnerability to inflammation. These associations between alexithymia and interoceptive processing might suggest that differences in interoceptive abilities could trigger distinct pathophysiological processes within the brain, which may predispose to a different set of clinical manifestations.

Previous research has linked heightened visceral hypersensitivity and amplified interoceptive transmission to CD [33]. Recently, Atanasova *et al* [6] found that IBD patients report increased emotional awareness and a greater tendency to distract themselves from unpleasant sensations, and revealed significant associations between interoceptive sensibility and emotional processing. However, contrary to our study, they failed to detect any differences in cardiac interoceptive accuracy between IBD patients and healthy controls. Our investigation was characterized by a different methodological design, including measures of both cardiac and gastric interoception and a separate data analysis for CD and UC patients, which allowed us to detect statistically significant differences in interoceptive accuracy and sensibility scores between patients and controls. Both groups of IBD patients exhibited a heightened gastric interoceptive accuracy that was significantly correlated with the severity of several GI symptoms, including gas and bloating, constipation and incontinence. These findings provide further evidence of a hyper-aroused (atypical) neuronal network conveying interoceptive information from the GI tract to the brain, which renders IBD patients extremely sensitive to gut-derived physiological alterations and makes those patients more likely to experience them as distressing, somatic symptoms. There is strong neuroimaging evidence that CD and UC patients display altered connectivity in brain regions implicated in interoceptive processing, such as the insular cortex and the anterior cingulate gyrus [34,35]. Furthermore, in CD patients, interoceptive sensibility was significantly associated with levels of CRP and proinflammatory cytokines IL-1β and IL-6, corroborating previous research supporting a connection between inflammatory processes and interoceptive signaling [36]. Elevated IL-1β and IL-6 levels have been implicated in IBD pathogenesis [37], but to our knowledge this is the first investigation to report significant associations between interoception and levels of serum proinflammatory cytokines in IBD patients. Although the present study's cross-sectional design does not allow us to safely establish whether inflammation triggers interoceptive transmission or *vice versa*, it seems that the interoceptive circuitry constitutes a key part of the gut-brain axis.

Another interesting finding was that UC patients had greater cardiac interoceptive accuracy and different interoceptive sensibility compared to healthy controls and CD patients. Several investigations have detected significant differences at a clinical and pathophysiological level between CD and UC. A recent study revealed that CD and UC patients have distinct affective temperament profiles, suggesting that the presence of mood or anxiety disorders may originate from different pathogenetic pathways [28]. Similarly, our findings suggest potential differences in domain-specific interoceptive abilities between UC and CD.

UC patients exhibited a discrepancy between actual and perceived interoceptive abilities that could lead to more prediction errors regarding bodily internal states, a condition that might compromise body homeostasis. According to recent computational theories, the brain processes information in a Bayesian manner, making predictions about its external and internal environment, and regulates homeostasis by minimizing prediction errors [38]. UC patients experienced amplified interoceptive signaling, but felt less confident in interpreting and integrating the body's internal state, thus experiencing the emergence of cardiac or gastric internal sensations as more ambiguous and threatening. In states of gut-derived inflammation, where there is an activation of bottom-up interoceptive signaling through the vagus nerve [39] and cytokine release [40], it is possible that the brain will react with a cascade of top-down signals that might underlie the vicious cycle of autoimmunity, the exacerbation of clinical symptomatology and the deterioration of quality of life.

The present study's main limitation was the relatively small sample size, which did not allow us to perform regression analysis to seek independent predictors of symptom and disease severity. Another limitation was the cross-sectional design, which did not permit the drawing of safe conclusions about causality in the observed associations. Finally, our sample did not include patients with another type of chronic GI disease. For example, comparing IBD patients with patients with functional GI disease would further elucidate the connection between alexithymia, interoception and intestinal inflammation. For this reason, future prospective investigations with larger sample sizes, including patients with functional GI disease, are needed to corroborate and expand existing findings.

In conclusion, IBD patients reported more alexithymic traits and better gastric interoception, which were linked to GI symptom severity, body image disturbance and disease activity indices. A distinct pattern of interoceptive processing was observed in UC patients compared to healthy controls and CD patients, suggesting that in conditions of allostatic load (intestinal dysbiosis or/and inflammation) this patient group might be more prone to react in a maladaptive way, leading to greater somatization and perpetuation of autoimmunological processes. Our study confirmed the presence of significant intercorrelations between emotional and interoceptive processing difficulties and provided evidence that they are associated with disease severity and the degree of inflammation, suggesting that these processes might be implicated in IBD pathophysiology. Our data-driven hypothesis is that interoceptive circuits constitute a key mediator in the pathway between constitutional deficits in emotional processing and the emergence of psychosomatic suffering. Exploring in greater depth the involvement of interoceptive processing in the gut-brain crosstalk in the context of intestinal dysbiosis and low-grade inflammation might provide new targets for intervention in an attempt to regulate autoimmunity and restore gut homeostasis.

Summary Box

What is already known:

- Emotional processing deficits in the form of alexithymia increase the risk of stress-mediated somatization and disturbed autoimmunity and may eventually lead to physical and psychological morbidity
- Inflammatory bowel disease (IBD) is characterized by a complex interplay between intestinal inflammatory processes and bottom-up neurophysiological circuitry that underlies gut-brain communication and regulates body homeostasis
- There is emerging evidence that chronic gastrointestinal disease patients exhibit disturbed emotional processing, heightened visceral hypersensitivity and amplified interoceptive transmission

What the new findings are:

- Increased alexithymic characteristics and atypical interoceptive signaling were prevalent in IBD patients
- These emotional and interoceptive processing difficulties were associated with disease severity and activity and the degree of inflammation, suggesting that they might be implicated in IBD pathophysiology
- Interoceptive circuits probably mediate the association between constitutional deficits in emotional processing and the emergence of IBD symptomatology
- Interoception-altering interventions might provide significant clinical benefits for IBD patients and should be tested as potential treatment strategies

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Supplementary material

Supplementary Table 1 Between group comparisons in psychological distress, gastrointestinal symptom presence and impact and body image

Parameters	CD patients	UC patients	Healthy controls	P-value for comparisons		
				CD vs. UC	CD vs. controls	UC vs. controls
HADS-A, median (IQR)	6.0 (5.0-9.5)	8.0 (5.3-12.8)	4.0 (2.0-7.25)	0.252	0.032	0.008
HADS-D, median (IQR)	6.0 (3.5-9.0)	6.0 (4.3-9.8)	4.0 (1.0-6.25)	0.756	0.003	0.008
Nausea presence, yes, N (%)	11 (27.5)	6 (40.0)	5 (10.2)	0.372	0.035	0.007
Vomiting presence, yes, N (%)	4 (10.0)	1 (6.7)	5 (10.2)	0.702	0.975	0.681
Abdominal pain presence, median (IQR)	22 (55.0)	7 (46.7)	12 (24.0)	0.581	0.003	0.090
Abdominal pain-associated impairment, N (%)				0.602	0.053	0.083
Not at all	26 (65.0)	9 (60.0)	43 (86.0)			
A little	10 (25.0)	3 (20.0)	4 (8.0)			
A lot	4 (10.0)	3 (20.0)	3 (6.0)			
Diarrhea presence, yes, N (%)	31 (77.5)	11 (73.3)	18 (36.0)	0.746	<0.001	0.011
Diarrhea-associated impairment, N (%)				0.408	<0.001	0.011
Not at all	25 (62.5)	11 (73.3)	48 (96.0)			
A little	12 (30.0)	2 (13.3)	2 (4.0)			
A lot	3 (7.5)	2 (13.3)	0 (0.0)			
Bloating presence, yes, N (%)	24 (64.9)	11 (73.3)	35 (72.9)	0.555	0.424	0.975
Bloating-associated impairment, N (%)				0.816	0.296	0.139
Not at all	20 (54.1)	7 (46.7)	28 (58.3)			
A little	12 (32.4)	5 (33.3)	18 (37.5)			
A lot	5 (13.5)	3 (20.0)	2 (4.2)			
Constipation presence, yes, N (%)	23 (59.0)	7 (46.7)	23 (46.0)	0.415	0.224	0.964
Constipation-associated discomfort, N (%)				0.125	0.636	0.041
Not at all	30 (76.9)	15 (100.0)	34 (68.0)			
A little	7 (17.9)	0 (0.0)	13 (26.0)			
A lot	2 (5.1)	0 (0.0)	3 (6.0)			
Incontinence presence, N (%)	7 (17.5)	3 (20.0)	2 (4.0)	0.830	0.034	0.041
Body image scale, median (IQR)	2.0 (0.0-7.0)	8.5 (2.5-13.5)	1.0 (0.0-4.0)	0.016	0.547	<0.001

HADS-A, hospital anxiety and depression scale-anxiety; HADS-D, hospital anxiety and depression scale-depression; CD, Crohn's disease; UC, ulcerative colitis; IQR, interquartile range

Supplementary Table 2 Correlations between alexithymia traits, psychological distress, body image and gastrointestinal symptom severity in patients with inflammatory bowel disease

Parameters	DIF		DDF		EOT		TAS total	
	CD	UC	CD	UC	CD	UC	CD	UC
HADS-A								
r	0.288	0.025	0.220	0.130	0.131	-0.475	0.311	-0.071
P-value	0.104	0.926	0.219	0.632	0.468	0.063	0.078	0.794
HADS-D								
r	0.062	0.367	0.085	0.031	-0.098	-0.316	0.056	0.100
P-value	0.731	0.162	0.638	0.910	0.587	0.233	0.758	0.712
BIS total								
r	0.570	0.297	0.350	-0.096	0.019	-0.521	0.428	-0.012
P-value	<0.001	0.264	0.029	0.723	0.910	0.038	0.007	0.965
Nausea presence, median (IQR)								
Yes	24 (19-25)	15.5 (12-20.5)	15 (14-18)	16 (13-20.5)	22 (17-25)	22 (18.8-24)	61 (53-68)	49.5 (48-65.8)
No	13 (9.5-22)	16 (11.5-25)	12 (9-17)	14 (9.5-16.5)	20 (15.5-23)	22 (17-23.5)	46 (38-58)	49 (43-60.5)
P-value	0.015	0.722	0.177	0.171	0.438	0.858	0.045	0.408
Vomiting presence, median (IQR)								
Yes	23 (14.3-28)	19	16 (11-20.3)	22	18.5 (14.3-24)	30	57 (41-71.5)	71
No	18 (10.3-23.8)	15 (11.8-25)	13.5 (9.3-17)	14 (9.8-17.5)	20 (16.3-24)	22 (18-23)	49 (40.5-61)	49 (44.8-59.3)
P-value	0.190	0.642	0.391	0.101	0.717	0.101	0.484	0.104
Abdominal pain presence, median (IQR)								
Yes	21.5 (12.8-25)	19 (14-25)	15.5 (11.5-19)	14 (10-20)	19.5 (15-22.5)	22 (16-23)	58 (39.3-65)	49 (45-64)
No	12 (9.8-20.5)	14.5 (11-20.8)	12 (9-15.3)	14 (10.3-18)	21 (16-24.5)	22 (19-23.8)	45.5 (41.3-56)	49.5 (45-57.5)
P-value	0.031	0.269	0.051	0.770	0.375	0.482	0.118	0.816
Abdominal pain-associated impairment, median (IQR)								
Not at all	13 (10-22)	13 (10.5-19.5)	12.5 (9.8-17)	14 (11.5-19)	20.5 (15.8-24)	22 (18.5-23.5)	46.5 (39.8-58)	49 (45-57)
A little	23.5 (18.8-25.8)	25 (25-)	17 (13.8-21.3)	14 (11-)	20 (17.3-22.5)	22 (13-)	61 (52.5-69.3)	63 (49-)
A lot	13 (9.5-25.5)	14 (14-)	9.5 (5.5-18.8)	10 (9-)	18 (10.3-23.5)	22 (18-)	39.5 (26.8-67.3)	45 (42-)
P-value	0.114	0.042	0.078	0.922	0.674	0.858	0.095	0.505
Diarrhea presence, median (IQR)								
Yes	20 (11-25)	19 (11-25)	13 (9-18)	14 (10-20)	20 (17-24)	22 (18-23)	53 (40-63)	49 (45-64)
No	13 (10.5-21.5)	14.5 (12.3-17)	14 (10.5-16.5)	14 (7.3-14.8)	20 (15.5-25)	20.5 (18.3-25)	47 (41-57)	49.5 (39-54.5)
P-value	0.417	0.431	0.948	0.428	0.961	0.947	0.638	0.512
Diarrhea-associated impairment, median (IQR)	18 (10-23)	16 (11-25)	13 (10-16.5)	15 (11-20)	20 (15-24)	22 (18-24)	47 (39.5-58)	49 (46-64)
Not at all	21 (12-24.8)	20 (14-)	16.5 (12-18.8)	12 (10-)	20 (18.3-24.3)	20.5 (18-)	61 (44.5-63.8)	52.5 (42-)
A little	11 (9-)	18 (14-)	7 (5-)	11.5 (9-)	19 (8-)	22 (22-)	35 (24-)	51.5 (45-)
A lot	0.689	0.593	0.300	0.377	0.685	0.975	0.282	0.920
P-value								

(*Contd...*)

Supplementary Table 2 (*Continued*)

Parameters	DIF		DDF		EOT		TAS total	
	CD	UC	CD	UC	CD	UC	CD	UC
Bloating presence, median (IQR)								
Yes	21.5 (12-25)	19 (13-25)	15 (10.3-18)	14 (10-19)	20 (18.3-23.5)	22 (18-23)	58 (42.3-63.8)	50 (45-64)
No	13 (7.5-22)	13.5 (10.3-17)	13 (10.5-16)	14 (10-18.5)	20 (15-25)	21.5 (18-25.5)	45 (39.5-54.5)	49 (45.3-54.3)
P-value	0.074	0.168	0.545	0.895	0.949	0.597	0.186	0.512
Bloating-associated impairment, median (IQR)								
Not at all	14 (8.5-22)	16 (10-22)	13.5 (11-17)	14 (14-20)	19 (15-23.5)	22 (8-24)	46 (40.5-58)	49 (46-58)
A little	21 (13.5-25)	14 (12.5-25.5)	14.5 (10.5-18)	11 (7.5-14.5)	20 (18.3-23.5)	19 (15.5-22.5)	57 (44.3-62.5)	49 (39-56.5)
A lot	21 (10-28.5)	19 (14-)	18 (6-23)	17 (9-)	20 (13.5-27)	22 (22-)	68 (29.5-74)	64 (45-)
P-value	0.340	0.544	0.781	0.300	0.886	0.342	0.556	0.387
Constipation presence, median (IQR)								
Yes	20 (10-25)	16 (14-25)	12 (7-17)	11 (9-14)	19 (15-22)	23 (18-24)	53 (35-61)	49 (44-63)
No	18 (11.3-23.3)	15 (10.5-21.3)	15.5 (12.3-18)	16 (14-20)	22 (19.3-26)	20.5 (18.3-22)	53.5 (44.3-66.3)	49.5 (46.8-63)
P-value	0.875	0.295	0.076	0.079	0.029	0.412	0.331	0.642
Constipation-associated discomfort, median (IQR)								
Not at all	18 (11-24)		14 (10.8-18)		20 (17.8-24.3)		49 (42-61.5)	
A little	20 (7-27)		15 (6-17)		20 (15-24)		58 (28-71)	
A lot	18.5 (12-)		12 (10-)		14.5 (14.0-)		45 (37-)	
P-value	0.930	-	0.780	-	0.226	-	0.679	-
Incontinence presence, median (IQR)								
Yes	12.0 (11.0-25.0)	22.0 (19.0-)	9.0 (7.0-13.0)	19.0 (14.0-)	20.0 (15.0-25)	23.0 (22.0-)	46.0 (32.0-53.0)	67.0 (58.0-)
No	19.0 (10.5-24.0)	14.0 (11.3-23.0)	15 (11.5-17.5)	14.0 (9.3-16.5)	20.0 (16.5-24)	20.5 (18.0-22.8)	56.0 (42.0-62.0)	49.0 (44.3-54.5)
P-value	0.762	0.147	0.049	0.126	0.734	0.108	0.240	0.020

DIF, difficulty identifying feelings subscale; DDF, difficulty describing feelings subscale; EOT, externally oriented thinking subscale; TAS, Toronto alexithymia scale; CD, Crohn's disease; UC, ulcerative colitis; HADS-A, hospital anxiety and depression scale-anxiety; HADS-D, hospital anxiety and depression scale-depression; BIS, body image Scale; IQR, interquartile range

Supplementary Table 3 Correlations between interoceptive accuracy, psychological distress, body image, alexithymia and disease activity

Scores	Cardiac interoception		Water volume to satiety		Water volume to discomfort		Total water volume	
	CD	UC	CD	UC	CD	UC	CD	UC
HADS-A								
r	-0.288	-0.117	-0.103	-0.143	0.020	-0.277	0.014	-0.275
P-value	0.104	0.667	0.575	0.597	0.917	0.298	0.940	0.302
HADS-D								
r	-0.009	0.150	0.075	-0.278	0.005	0.043	0.058	-0.139
P-value	0.961	0.579	0.685	0.298	0.979	0.875	0.756	0.606
Body Image Scale								
r	0.009	-0.237	-0.091	0.128	-0.041	0.013	-0.036	0.159
P-value	0.955	0.376	0.616	0.637	0.822	0.961	0.846	0.558
DIF								
r	-0.145	0.057	0.060	-0.267	0.156	0.328	0.157	0.099
P-value	0.370	0.834	0.734	0.317	0.386	0.215	0.384	0.714
DDF								
r	-0.264	-0.458	-0.066	-0.590	0.137	0.107	0.077	-0.155
P-value	0.100	0.075	0.712	0.016	0.449	0.693	0.669	0.566
EOT								
r	-0.443	0.028	0.021	-0.193	0.265	0.460	0.206	0.228
P-value	0.004	0.917	0.908	0.473	0.136	0.073	0.250	0.396
TAS total								
r	-0.313	-0.359	0.018	-0.613	0.205	0.375	0.164	0.022
P-value	0.049	0.172	0.919	0.011	0.252	0.152	0.361	0.935
Crohn's disease activity (Harvey-Bradshaw Index)								
Clinical remission, median (IQR)	0.53 (0.0-0.77)		155 (119-263)		380 (143-500)		640 (298-750)	
Mild-to-moderate disease median (IQR)	0.22 (0.0-0.58)		200 (110-210)		385 (205-500)		530 (330-740)	
P-value	0.090		0.709		0.750		0.843	
UC disease activity (Truelove-Witts Index)								
Mild, median (IQR)	0.68 (0.0-0.86)		60 (140-325)		315 (50-425)		640 (140-725)	
Moderate, median (IQR)	0.71 (0.22-0.83)		250 (105-300)		500 (335-638)		770 (460-908)	
P-value	0.465		0.570		0.062		0.220	

HADS-A, hospital anxiety and depression scale-anxiety; HADS-D, hospital anxiety and depression scale-depression; DIF, difficulty identifying feelings subscale; DDF, difficulty describing feelings subscale; EOT, externally oriented thinking subscale; TAS, Toronto alexithymia scale; CD, Crohn's disease; UC, ulcerative colitis; IQR, interquartile range

Supplementary Table 4 Correlations between interoceptive accuracy and gastrointestinal symptom severity

Parameters	Cardiac interoception		Water volume to satiety		Water volume to discomfort		Total water volume	
	CD	UC	CD	UC	CD	UC	*CD*	*UC*
Nausea presence, median (IQR)								
Yes	0.15 (0.0-0.64)	0.51 (0.0-0.68)	173 (124-280)	173 (83-298)	410 (299-536)	320 (38-516)	653 (450-760)	620 (125-728)
No	0.44 (0.0-0.73)	0.80 (0.43-0.84)	155 (111-240)		385 (190-500)		530 (320-740)	
P-value	0.625	0.059	0.520	0.140	0.583	0.480	*0.378*	*0.287*
Vomiting presence, median (IQR)								
Yes	0.38 (0.0-0.78)	0.71 (0.71-0.71)	160 (125-)	100 (100-100)	440 (120-)	500 (500-500)	565 (280-)	600 (600-600)
No	0.28 (0.0-0.67)	0.61 (0.28-0.81)	150 (115-250)	250 (140-303)	383 (209-508)	398 (193-516)	548 (345-759)	640 (496-755)
P-value	0.778	0.817	0.784	0.164	0.754	0.487	*0.851*	*0.642*
Abdominal pain presence								
Yes	0.17 (0.0-0.74)	0.78 (0.68-0.83)	160 (120-275)	260 (140-325)	375 (201-536)	415(315-500)	548 (328-808)	640 (600-720)
No	0.45 (0.0-0.66)	0.40 (0.02-0.74)	150 (115-250)	240 (118-273)	430 (240-500)	368 (90-569)	565 (360-740)	643 (185-814)
P-value	0.799	0.049	0.945	0.324	0.871	0.908	*0.651*	*0.908*
Abdominal pain-associated impairment								
Not at all	0.41 (0.0-0.72)	0.46 (0.05-0.79)	150 (120-250)	250 (125-270)	440 (240-500)	380 (130-553)	565 (360-740)	640 (230-793)
A little	0.17 (0.0-0.70)	0.80 (0.55-)	180 (121-269)	205 (140-)	350 (206-688)	460 (415-)	510 (335-956)	720 (555-)
A lot	0.31 (0.0-0.74)	0.71 (0.68-)	50 (0-)	325 (100-)	275 (170-)	315 (140-)	485 (220-)	640 (600-)
P-value	0.985	0.208	0.527	0.589	0.617	0.641	*0.900*	*0.894*
Diarrhea presence								
Yes	0.46 (0.0-0.72)	0.71 (0.34-0.83)	150 (119-281)	250 (140-310)	380 (198-515)	415 (210-500)	565 (325-770)	640 (555-725)
No	0.0 (0.0-0.60)	0.49 (0.12-0.74)	173 (113-240)	240 (80-273)	408 (333-500)	415 (115-715)	513 (468-734)	655 (200-983)
P-value	0.194	0.327	0.760	0.556	0.801	0.695	*0.900*	*0.896*
Diarrhea-associated impairment								
Not at all	0.37 (0.0-0.73)	0.55 (0.10-0.80)	160 (118-250)	250 (140-280)	450 (225-500)	460 (310-520)	565 (340-745)	720 (560-770)
A little	0.34 (0.0-0.74)	0.89 (0.83-)	160 (125-370)	233 (140-)	330 (205-645)	365 (315-)	565 (350-790)	598 (555-)
A lot	0.0 (0.0-)	0.51 (0.34-)	25 (0.0-)	305 (110-)	170 (170-170)	175 (140-)	220 (220-220)	480 (320-)
P-value	0.619	0.117	0.060	0.840	0.414	0.263	*0.330*	*0.496*
Bloating presence								
Yes	0.17 (0.0-0.67)	0.68 (0.34-0.80)	135 (113-190)	250 (140-310)	330 (185-500)	415 (310-515)	460 (315-740)	640 (560-750)
No	0.44 (0.0-0.71)	0.63 (0.12-0.84)	210 (166-288)	210 (58-295)	500 (38-523)	238 (13-691)	720 (539-776)	433 (95-976)
P-value	0.947	0.948	0.029	0.647	0.122	0.514	*0.054*	*0.694*
Bloating-associated impairment								
Not at all	0.45 (0.0-0.70)	0.46 (0.10-0.81)	200 (125-250)	250 (110-280)	490 (320-500)	380 (50-585)	685 (495-750)	640 (140-835)
A little	0.17 (0.0-0.74)	0.80 (0.26-0.89)	145 (118-219)	250 (185-318)	350 (188-671)	415 (313-490)	475 (310-849)	640 (558-760)
A lot	0.0 (0.0-0.31)	0.68 (0.55-)	50 (0-)	205 (100-)	188 (170-)	500 (140-)	275 (220-)	640 (600-)
P-value	0.263	0.696	0.047	0.682	0.173	0.895	*0.106*	*0.966*

(*Contd...*)

Supplementary Table 4 (*Continued*)

Parameters	Cardiac interoception		Water volume to satiety		Water volume to discomfort		Total water volume	
	CD	UC	CD	UC	CD	UC	*CD*	*UC*
Constipation presence								
Yes	0.46 (0.0-0.68)	0.81 (0.68-0.86)	155 (116-240)	300 (250-325)	430 (185-530)	425 (315-585)	530 (315-750)	725 (640-835)
No	0.0 (0.0-0.77)	0.49 (0.09-0.67)	155 (118-363)	173 (103-245)	383 (233-500)	345 (90-511)	603 (353-759)	580 (185-700)
P-value	0.506	0.021	0.587	0.011	0.956	0.298	*0.729*	*0.048*
Constipation-associated discomfort								
Not at all	0.17 (0.0-0.72)		148 (119-220)		380 (225-500)		565 (345-745)	
A little	0.37 (0.0-0.64)		205 (64-300)		460 (189-650)		600 (328-950)	
A lot	0.77 (0.76-)		205 (160-)		310 (120-)		515 (280-)	
P-value	0.181	-	0.828	-	0.617	-	*0.708*	-
Incontinence presence								
Yes	0.61 (0.0-0.76)	0.34 (0.10-)	135 (65-325)	110 (100-)	190 (133-248)	500 (210-)	300 (235-560)	600 (320-)
No	0.19 (0.0-0.66)	0.73 (0.48-0.82)	155 (120-250)	255 (156-308)	440 (240-515)	398 (183-501)	565 (360-768)	640 (556-744)
P-value	0.517	0.248	0.630	0.129	0.031	0.470	*0.061*	*0.885*

CD, Crohn's disease; UC, ulcerative colitis; IQR, interquartile range

Supplementary Table 5 Associations between interoceptive sensibility and anxiety, depression, body image and disease activity

MAIA	CD		UC		HADS-D				Body Image Scale				CD activity (Harvey-Bradshaw Index)		UC disease activity (Truelove-Witts Index)	
					CD		UC		CD		UC		In remission, median (IQR) Mild-to-moderate disease, median (IQR)		Mild, median (IQR) Moderate, median (IQR)	
	r	P-value	r	P-value	r	P-value	r	P-value	r	P-value	r	P-value	r	P-value	r	P-value
Noticing	0.549	0.001	0.082	0.764	0.356	0.042	0.243	0.363	0.356	0.026	0.402	0.122	2.8 (1.8-4.4) 2.6 (1.3-4.2)	0.759	2.5 (1.8-4.5) 3.3 (2-4)	0.869
Not distracting	0.210	0.241	-0.437	0.091	0.234	0.191	-0.192	0.477	0.092	0.578	-0.107	0.694	1.7 (1-2.6) 1.7 (1.1-3.1)	0.781	2.3 (2-3) 1.7 (1-3.5)	0.414
Not worrying	-0.407	0.019	-0.122	0.653	-0.154	0.391	0.022	0.935	-0.405	0.010	-0.239	0.373	2.7 (2.1-3) 2.7 (1.2-4.6)	0.951	2.7 (1.7-4) 2.3 (1.3-3.8)	0.622
Attention regulation	0.208	0.246	0.221	0.411	0.185	0.301	0.194	0.471	-0.045	0.784	0.084	0.757	3.1 (1.9-3.9) 2.9 (2.6-3.1)	0.243	2.9 (2-4.1) 2.6 (1.1-3.3)	0.462
Emotional awareness	0.452	0.008	0.101	0.710	0.316	0.073	0.316	0.233	0.209	0.201	0.516	0.041	3.8 (2.2-4.4) 3.6 (3-4.5)	0.830	2.4 (2-4.4) 3.6 (1.7-4.5)	0.463
Self-regulation	0.102	0.572	0.152	0.573	-0.045	0.804	0.277	0.300	-0.017	0.917	0.113	0.676	2.6 (1.4-3.7) 2.5 (1.7-3.8)	0.975	2.3 (1.3-3.5) 0.8 (0-4)	0.371
Body listening	0.186	0.301	-0.021	0.939	0.005	0.979	0.235	0.382	-0.004	0.981	0.580	0.019	2.7 (1.7-3.7) 2.7 (2.3-3.3)	0.975	2 (1.7-2.7) 3.7 (1.3-4.3)	0.253
Trusting	-0.448	0.010	-0.571	0.021	-0.218	0.230	-0.289	0.277	-0.419	0.009	-0.208	0.438	4 (3.7-5) 4.2 (3.3-5)	0.925	3 (2-4.7) 2.7 (2.5-4.2)	0.876

MAIA, multidimensional assessment of interoceptive awareness; HADS-A, hospital anxiety and depression scale-anxiety; HADS-D, hospital anxiety and depression scale-depression; CD, Crohn's disease; UC, ulcerative colitis; IQR, interquartile range

Supplementary Table 6 Associations between interoceptive sensibility and alexithymia

MAIA	DIF				DDF				EOT				TAS total			
	CD		UC		CD		UC		CD		UC		CD		UC	
	r	P-value	r	P-value	r	P-value	r	P-value	r	P-value	r	P-value	r	P-value	r	P-value
Noticing	0.004	0.979	0.038	0.889	0.134	0.409	-0.423	0.103	-0.173	0.285	-0.224	0.404	0.018	0.914	-0.324	0.221
Not distracting	0.084	0.606	-0.371	0.157	-0.079	0,630	-0.081	0.765	0.200	0.215	0.047	0.863	0.105	0.521	-0.164	0.545
Not worrying	-0.349	0.027	-0.138	0.611	-0.378	0.016	0.294	0.270	-0.052	0.750	-0.104	0.702	-0.342	0.031	0.042	0.878
Attention regulation	-0.395	0.012	0.111	0.681	-0.324	0.042	-0.110	0.685	-0.141	0.385	-0.209	0.437	-0.327	0.039	-0.159	0.557
Emotional awareness	-0.151	0.351	0.409	0.115	-0.104	0.525	-0.278	0.297	-0.170	0.293	-0.240	0.370	-0.175	0.279	-0.012	0.965
Self-regulation	-0.383	0.015	0.175	0.517	-0.279	0.081	-0.119	0.660	-0.186	0.250	-0.057	0.833	-0.345	0.029	-0.030	0.911
Body listening	-0.401	0.010	0.427	0.099	-0.343	0.030	-0.313	0.238	-0.110	0.499	-0.235	0.380	-0.359	0.023	-0.016	0.954
Trusting	-0.368	0.021	0.249	0.353	-0.355	0.027	-0.264	0.323	-0.016	0.921	0.495	0.051	-0.305	0.059	0.096	0.724

MAIA, multidimensional assessment of interoceptive awareness; DIF, difficulty identifying feelings subscale; DDF, difficulty describing feelings subscale; EOT, externally oriented thinking subscale; TAS, Toronto alexithymia scale; CD, Crohn's disease; UC, ulcerative colitis

Supplementary Table 7 Associations between interoceptive sensibility and gastrointestinal symptom severity and CRP levels

Parameters	MAIA Noticing		MAIA Not distracting		MAIA Not worrying		MAIA Attention regulation	
	CD	UC	CD	UC	CD	UC	CD	UC
Nausea presence, median (IQR)								
Yes	3.8 (2.8-4.3)	2.9 (1.1-3.8)	1.7 (1-2)	2 (0.9-2.5)	2 (1.3-2.3)	2.5 (1.4-3.8)	3.4 (3-3.6)	2.4 (1.8-3.2)
No	2.8 (1.6-3.8)	3.3 (2.1-3.9)	1.7 (1-2.5)	2 (1-3.2)	2.7 (1.8-3.3)	2.3 (1.5-3.8)	3 (1.6-3.9)	2.7 (1.2-3.3)
P-value	0.197	0.635	0.951	0.859	0.018	0.953	0.295	0.859
Vomiting presence, median (IQR)								
Yes	3.5 (2.9-4.7)	1.5 (1.5-1.5)	1.8 (0.9-2.3)	0.7 (0.7-0.7)	2.3 (1.8-2.3)	4 (4-4)	3.3 (3-3.5)	1.3 (1.3-1.3)
No	2.9 (1.6-3.9)	3.3 (2.3-3.8)	1.7 (1-2.3)	2 (1.3-3)	2.7 (1.7-3.3)	2.3 (1.6-3.7)	3 (1.7-3.7)	2.6 (1.8-3.3)
P-value	0.278	0.244	0.928	0.201	0.497	0.162	0.512	0.296
Abdominal pain presence								
Yes	3.7 (2.8-4.3)	3.5 (2.5-4.5)	1.7 (0.9-2)	1.3 (0.7-2)	2 (1.3-2.4)	2.3 (2-4)	3.3 (2.2-3.8)	2.9 (2.3-4.1)
No	2.3 (0.9-3.5)	2.9 (0.4-3.6)	1.8 (1-2.7)	2.7 (1.8-3.3)	3 (2.6-3.3)	2.2 (1.4-3.7)	2.9 (1.6-3.5)	2.3 (1.2-2.8)
P-value	0.024	0.294	0.179	0.020	0.003	0.641	0.269	0.131
Abdominal pain-associated impairment								
Not at all	2.6 (1.1-3.8)	2.5 (0.9-3.5)	1.7 (0.9-2.4)	2.3 (1.8-3.2)	2.7 (1.9-3.3)	2.7 (1.5-3.8)	3 (1.6-3.6)	2.6 (1.2-2.9)
A little	3.8 (2.8-4.6)	3.5 (2.5-3.5)	1.7 (1-2.2)	1 (0.3-1)	1.8 (0.8-2.5)	2.3 (2-2.3)	3.3 (2.2-3.8)	2.6 (2.3-2.6)

(*Contd...*)

Supplementary Table 7 (*Continued*)

Parameters	MAIA Noticing		MAIA Not distracting		MAIA Not worrying		MAIA Attention regulation	
	CD	UC	CD	UC	CD	UC	CD	UC
A lot	3.4 (2.9-4.1)	4.5 (1.5-4.5)	1.5 (0.8-2.2)	1.7 (0.7-1.7)	2.2 (1.8-2.6)	2.7 (0.7-2.7)	3.5 (3.2-4.2)	4.1 (1.3-4.1)
P-value	0.076	0.384	0.874	0.042	0.055	0.908	0.216	0.387
Diarrhea presence								
Yes	2.8 (1.5-3.8)	3.3 (2.5-4)	1.7 (1-2.3)	1.7 (1-2.3)	2.3 (1.7-3)	2.3 (1.7-4)	3 (2-3.7)	2.6 (1.3-3.3)
No	3.5 (2.3-4.4)	1.3 (0-3.4)	1.7 (1.7-2.5)	2.7 (1.1-3.3)	2.3 (1.8-3)	2.2 (0.9-3.4)	3 (2.1-3.4)	2.4 (1.4-2.8)
P-value	0.291	0.148	0.247	0.325	0.845	0.510	0.615	0.471
Diarrhea-associated impairment								
Not at all	2.8 (1.5-3.9)	2.5 (1.5-3.3)	1.7 (1-2.3)	2 (1-3)	2.7 (2-3.3)	2.3 (1.7-4)	2.9 (1.6-3.3)	2.6 (1.3-2.9)
A little	3.4 (2.8-4.3)	4 (3.5-4)	1.7 (1-2.5)	1,2 (0.3-1.2)	1.8 (1.1-2.8)	2.3 (2-2.3)	3.5 (3-3.8)	3.8 (3.3-3.8)
A lot	3.5 (3.3-3.5)	4.3 (4-4.3)	1.3 (0.7-1.3)	3 (1.7-3)	2.3 (1.7-2.3)	2.2 (0.7-2.2)	3.6 (3.4-3.6)	2.6 (1-2.6)
P-value	0.341	0.025	0.889	0.400	0.105	0.864	0.029	0.145
Bloating presence								
Yes	3.5 (2.8-4.2)	3.5 (2.5-4)	1.8 (1-2.6)	1.7 (0.7-2)	2.2 (1.7-3)	2.3 (1.7-3.7)	3.2 (1.7-3.7)	2.6 (1.3-3.3)
No	2 (1.4-3.5)	0.9 (0-2.9)	1.7 (0.8-1.8)	2.7 (2.3-3.3)	3 (2.2-4.5)	2.7 (0.9-3.9)	3 (2.1-3.7)	2.6 (1.6-2.8)
P-value	0.079	0.030	0.369	0.042	0.049	0.948	0.774	0.844
Bloating-associated impairment								
Not at all	2.4 (1.3-3.8)	2.5 (0-3.3)	1.7 (0.8-2.3)	2.3 (2-3.3)	2.8 (2.1-3.6)	3.7 (1.3-4)	3 (1.6-3.5)	2.7 (1.3-2.9)
A little	2.9 (2.8-3.9)	3.5 (2.5-4.1)	1.8 (1-2.5)	1.3 (0.5-2.5)	1.8 (1.3-2.8)	2.3 (1.8-2.7)	3.2 (1.7-3.8)	2.6 (1.6-3.8)
A lot	3.8 (3.4-4.5)	3.5 (1.5-3.5)	2.3 (1-3)	1 (0.7-1)	2.3 (1.3-2.8)	2.3 (0.7-2.3)	3.6 (3.2-4.1)	2.3 (1.3-2.3)
P-value	0.123	0.314	0.467	0.039	0.066	0.894	0.267	0.970
Constipation presence								
Yes	2.8 (1.5-3.8)	3.3 (1.8-4.5)	1.7 (1-2.7)	1.7 (1.3-3)	2.7 (1.7-3)	2 (0.7-2.7)	3 (1.6-3.9)	3.3 (2.6-4.1)
No	3.4 (2-3.9)	2.9 (1.8-3.7)	1.7 (0.7-2.3)	2.2 (0.8-2.8)	2.3 (1.7-3.2)	3.2 (1.8-3.9)	3.1 (2.1-3.6)	2.1 (1.2-2.8)
P-value	0.422	0.683	0.358	0.816	0.556	0.129	0.954	0.037
Constipation-associated discomfort								
Not at all	2.9 (1.7-3.8)	3.3 (1.8-3.8)	1.7 (0.7-2.3)	2 (1-3)	2.3 (1.6-3.1)	2.3 (1.7-3.7)	3 (1.6-3.6)	2.6 (1.3-3.3)
A little	3.5 (1.5-4.8)	-	1.7 (1-2.7)	-	3 (2-3.7)	-	3 (2.6-4.2)	-
A lot	3.9 (2.8-3.9)	-	1.8 (1.7-.8)	-	2 (1.7-2)	-	3.1 (3-3.1)	-
P-value	0.414	-	0.851	-	0.299	-	0.756	-
Incontinence presence								
Yes	2.8 (2.5-4.3)	3.3 (1.5-3.3)	2 (0.7-2.7)	1.7 (0.7-1.7)	2 (1.7-2.7)	3.7 (1.3-3.7)	3 (2-3.4)	1.3 (1-1.3)
No	3 (1.6-3.9)	2.9 (1.9-3.7)	1.7 (1-2.3)	2 (1.1-2.8)	2.7 (1.7-3.2)	2.3 (1.7-3.4)	3 (1.9-3.8)	2.6 (2.1-3.2)
P-value	0.915	0.942	0.654	>0.999	0.421	0.513	0.592	0.311
CRP levels								
Normal, median (IQR)	3.5 (2.8-4.1)	2.9 (1.6-3.7)	1.7 (1-2.5)	2.2 (0.8-3)	2.3 (1.7-2.8)	2.5 (1.7-3.7)	3.1 (2.7-3.9)	2.6 (1.3-3.2)
Increased, median (IQR)	1.5 (0.9-2.9)	3.8 (2.8-4.4)	1.7 (1-2)	1.8 (1.2-2.5)	3 (2.3-3.7)	1.8 (0.8-3.6)	3 (2.1-3.6)	3.1 (2.4-3.9)
P-value	0.005	0.160	0.402	0.715	0.048	0.502	0.267	0.201

(*Contd...*)

Supplementary Table 7 (*Continued*)

Parameters	MAIA Emotional awareness		MAIA Self - regulation		MAIA Body listening		MAIA Trusting	
	CD	UC	CD	UC	CD	UC	CD	UC
Nausea presence, median (IQR)								
Yes	4.2 (3.4-4.6)	2.8 (1.8-4.4)	3.3 (2.3-4)	1.9 (0.8-2.8)	2.7 (2-2.7)	2.2 (0.8-2.8)	3.3 (2.7-4)	2.5 (2.3-3.5)
No	3.4 (2.4-4.3)	3.4 (2-4.1)	2.3 (1.6-3.4)	2.3 (1.4-4.1)	2.3 (1.2-3.5)	2.7 (1-3.5)	4.2 (3.4-5)	3.3 (2.2-4.2)
P-value	0.047	0.953	0.187	0.442	0.843	0.515	0.018	0.593
Vomiting presence, median (IQR)								
Yes	4.6 (4.2-4.8)	0.0(0-0)	3.5 (1.1-4)	0(0-0)	2.2 (1.5-4.1)	0(0-0)	3.5 (2.7-4.8)	2.7 (2.7-2.7)
No	3.5 (2.7-4.4)	3.3 (2.2-4.4)	2.5 (1.8-3.4)	2.4 (1.2-3.6)	2.5 (1.7-2.9)	2.3 (1.5-3.4)	4 (3.3-4.7)	2.8 (2.3-3.9)
P-value	0.055	0.130	0.512	0.131	0.964	0.104	0.725	0.907
Abdominal pain presence								
Yes	4 (3.4-4.6)	3.8 (2-4.4)	2.9 (1.7-3.8)	0.5 (0-3.8)	2.5 (1.3-2.8)	2.7 (2-3.7)	3.7 (2.8-4.3)	2.7 (2.3-3.7)
No	3.2 (2.2-4.4)	2.4 (2.1-3.4)	2.4 (1.7-3.5)	2 (1.1-2.9)	2.3 (1.9-3.1)	1.8 (0.5-2.6)	4.2 (3.3-5)	2.8 (2.1-4.3)
P-value	0.108	0.295	0.693	0.685	0.837	0.270	0.254	0.861
Abdominal pain-associated impairment								
Not at all	3.4 (2.2-4.4)	2.4 (2-3.3)	2.3 (1.5-3.6)	2 (1.1-2.8)	2.3 (1-3.1)	2 (0.7-2.5)	4.3 (3.3-5)	2.7 (2-4)
A little	3.9 (3.3-4.7)	3.8 (3.6-3.8)	2.9 (1.6-3.4)	2.5 (0-2.5)	2.5 (1.6-2.7)	3.3 (2.3-3.3)	3.5 (2.7-4)	2.3 (2.3-2.3)
A lot	4.4 (3.6-4.9)	4.4 (0-4.4)	3.1 (2.8-4.6)	3.5 (0-3.5)	2.8 (2.4-3.5)	2.7 (0-2.7)	3.8 (2.9-4)	3.7 (2.7-3.7)
P-value	0.154	0.232	0.346	0.872	0.419	0.328	0.109	0.385
Diarrhea presence								
Yes	3.6 (2.8-4.6)	3.6 (2-4.4)	2.8 (2-3.5)	2.5 (1.3-3.8)	2.3 (1.7-2.7)	2.7 (1.7-3.7)	4 (3.3-5)	3.3 (2.3-4.7)
No	4 (2.6-4.5)	2.3 (0.6-3)	2.3 (1.3-3.6)	1.5 (0.8-2.4)	2.7 (1.5-3.5)	1.2 (0.3-2.3)	4 (2.7-4.5)	2.5 (1.8-2.9)
P-value	0.733	0.148	0.581	0.239	0.514	0.116	0.578	0.212
Diarrhea-associated impairment								
Not at all	3 (2.2-4.3)	2.4 (2-3.4)	2.3 (1.5-3.6)	2 (0.8-2.5)	2.3 (1.2-3)	2 (0.3-2.3)	4.2 (3.3-4.9)	2.3 (2-3)
A little	3.8 (3.4-4.6)	4.1 (3.8-4.1)	3.1 (2.3-3.4)	4.1 (3.8-4.1)	2.5 (1.8-2.7)	3 (2.7-3)	3.7 (3.1-4.8)	3.7 (3.7-3.7)
A lot	4.6 (4.2-4.6)	4.7 (4.4-4.7)	3 (2.8-3)	4.3 (3.5-4.3)	3 (2.3-3)	4.5 (4-4.5)	3.7 (2.7-3.7)	5 (5-5)
P-value	0.058	0.029	0.266	0.016	0.477	0.029	0.500	0.025
Bloating presence								
Yes	3.8 (2.9-4.5)	3.6 (2.2-4.4)	2.8 (1.8-3.9)	2.5 (1-3.8)	2.5 (1.7-2.9)	2.7 (2-3.7)	3.7 (3.3-4.3)	3 (2.3-3.7)
No	3.4 (2.3-4.6)	2.2 (0.5-2.4)	2.3 (1.6-3.3)	1.6 (0.9-2.4)	2.3 (1.5-2.7)	1.3 (0.5-1.9)	4 (3-5)	2.5 (2.1-4.2)
P-value	0.503	0.066	0.364	0.295	0.748	0.067	0.549	0.599
Bloating-associated impairment								
Not at all	3.4 (2.1-4.4)	2.4 (2-3.4)	2.4 (1.6-3.4)	2.3 (1.3-3)	2.3 (1.1-2.7)	2 (1-2.7)	4.3 (3.3-5)	2.7 (2-4.7)
A little	3.7 (2.9-4.2)	3.6 (2.7-4.1)	2.5 (1.4-3.6)	2 (0.5-4.1)	2.2 (1.7-2.7)	2.7 (1.3-3.5)	3.7 (2.8-4)	3 (2-3.7)
A lot	4.6 (4-5)	4.4 (0-4.4)	3 (2.5-4.4)	2.5 (0-2.5)	3 (2.5-3.7)	2.3 (0-2.3)	3.7 (2.8-4.5)	2.7 (2.3-2.7)
P-value	0.053	0.472	0.373	0.973	0.166	0.709	0.133	0.905
Constipation presence								
Yes	3.4 (2.6-4.2)	3.6 (2-4.4)	2.5 (1.5-3.8)	3 (0.8-3.8)	2.3 (1.3-3)	2.7 (1.7-3.7)	4 (3.3-5)	3.7 (2.7-4.7)

(*Contd...*)

Supplementary Table 7 (*Continued*)

Parameters	MAIA Emotional awareness		MAIA Self - regulation		MAIA Body listening		MAIA Trusting	
	CD	UC	CD	UC	CD	UC	CD	UC
No	4.1 (3.4-4.6)	2.4 (2.1-4.1)	2.6 (1.8-3.5)	2.1 (1.1-2.5)	2.5 (1.7-2.7)	2 (0.5-2.3)	3.5 (2.8-4.6)	2.3 (2-2.9)
P-value	0.179	0.560	0.954	0.562	0.818	0.182	0.295	0.048
Constipation-associated discomfort								
Not at all	3.7 (2.8-4.5)	3.2 (2-4.4)	2.4 (1.8-3.3)	2.3 (1-3.5)	2.3 (1.7-2.7)	2.3 (1-3.3)	4 (3.3-4.8)	2.7 (2.3-3.7)
A little	3.4 (2.6-4.2)	-	3.3 (1.5-4)	-	2.7 (1-3.7)	-	4 (3.3-5)	-
A lot	4.4 (4-4.4)	-	2.3 (0.5-2.3)	-	3 (1.3-3)	-	3.5 (2.7-3.5)	-
P-value	0.491	-	0.722	-	0.764	-	0.892	-
Incontinence presence								
Yes	4.4 (3-4.6)	3.4 (0-3.4)	3 (1.8-4)	3 (0-3)	2.7 (2-3.3)	2.7 (0-2.7)	4.3 (3.3-4.7)	(2.7-3.3)
No	3.6 (2.6-4.3)	2.8 (2.1-4.3)	2.5 (1.6-3.5)	2.1 (1.1-3.3)	2.3 (1.5-2.7)	2.2 (1.2-3.2)	4 (3.3-4.9)	2.5 (2.1-3.7)
P-value	0.205	0.828	0.682	0.612	0.440	0.717	0.684	0.245
CRP levels								
Normal, median (IQR)	4.2 (3.4-4.6)	2.8 (2.1-3.8)	3 (1.6-3.9)	2 (0.8-3.6)	2.7 (1.5-3.7)	2.2 (0.5-3.2)	4 (3.1-4.3)	2.8 (2.3-3.7)
Increased, median (IQR)	3 (2.3-3.5)	4.2 (2.5-4.4)	2.3 (1.5-3)	2.4 (1.1-3.3)	2.3 (2.2-2.7)	3 (2.1-3.9)	4 (3.3-5)	2.5 (2.1-4.4)
P-value	0.005	0.247	0.175	0.808	0.535	0.248	0.607	0.714

MAIA, multidimensional assessment of interoceptive awareness; CD, Crohn's disease; UC, ulcerative colitis; CRP, C-reactive protein