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Cognitive And Behavioral Differences Between Subtypes In Refractory Irritable Bowel Syndrome

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Abstract

Irritable bowel syndrome (IBS) is a functional gastrointestinal syndrome consisting of different bowel pattern subtypes: diarrhea predominant (IBS-D), constipation predominant (IBS-C) and alternating (IBS-A). This paper aimed to identify whether (1) psychological factors implicated in the cognitive behavioral model of IBS were differentially associated with bowel pattern subtypes (2) whether there were differences in symptom severity and work and social adjustment across the IBS-subtypes. Analysis was conducted on baseline data of 557 individuals with refractory IBS recruited into the Assessing Cognitive Therapy in Irritable Bowel (ACTIB) randomized controlled trial. Correlations assessed the associations between psychological factors, stool patterns, symptom severity and work and social adjustment. Hierarchical regressions identified whether cognitive and behavioral factors were significantly associated with frequency of loose/watery stools, hard/lumpy stools and symptom severity while controlling for affective (anxiety and depression) and demographic factors (age, gender, symptom duration). One-way ANOVAs were conducted to assess differences across Rome III classified subtypes (IBS-A, D and C) in cognitive, behavioral, affective, severity and adjustment measures. Psychological factors were significantly associated with symptom severity and work and social adjustment. Increased avoidance behavior and unhelpful gastrointestinal (GI) cognitions were significantly associated with higher frequency of loose/watery stools. Increased control behaviors were associated with higher frequency of hard/lumpy stools. Cognitive and behavioral differences were significant across the Rome III classified IBS subtypes. There were no differences in anxiety, depression, overall symptom severity or work and social adjustment. The results are

discussed in terms of their utility in tailoring cognitive behavioral treatments to IBS subtypes.

Keywords: Irritable bowel syndrome; IBS; subtypes; gastrointestinal cognitions; avoidance behaviors; safety behaviors; cognitive behavioral therapy

Cognitive and Behavioral Differences Between Irritable Bowel Syndrome Subtypes

Irritable bowel syndrome (IBS) is a functional gastrointestinal syndrome characterized by abdominal pain and associated disruptions to bowel patterns. The aetiology of IBS is generally agreed to be of biopsychosocial origin as biological, psychological and social factors interact to cause and maintain IBS symptoms (Drossman, 1996; Drossman, 2016). Criteria have been developed over the years to diagnose IBS in the absence of any physiological markers. The most current diagnostic criteria are the Rome IV criteria (Drossman, 2016). Four IBS subtypes are classified on the basis of individuals' bowel pattern predominance: Constipation predominant (IBS-C), diarrhea predominant (IBS-D), alternating bowel pattern (IBS-A) or unclassified IBS (IBS-U) for individuals who do not fall into the other bowel pattern categories. The IBS subtypes are thought to be reflective of differential pathophysiological mechanisms that may be targeted by pharmacotherapeutic approaches (Krogsgaard, Engsbro, & Bytzer, 2013). It is unclear as to whether differentiation in bowel pattern subtypes is important in understanding the psychological processes that may be maintaining symptoms (Fond et al., 2014).

The predominant psychological treatment approach for IBS is cognitive behavioral therapy (CBT). A CBT model of IBS posits that affective factors (e.g. anxiety/worry), unhelpful gastrointestinal (GI) related cognitions and unhelpful behavioral responses perpetuate symptoms and impact quality of life (Blanchard et al., 1992; Hutton, 2005; Kennedy et al., 2005; Spence & Moss-Morris, 2007). An example of an unhelpful illness-related cognition is "*it is embarrassing to keep going to the toilet*". Unhelpful behavioral responses to IBS symptoms may include avoidance behaviors such as avoiding certain foods or social occasions, or control

behaviors such as excessive straining on the toilet or carrying extra items when leaving the house in case of symptoms (Reme, Darnley, Kennedy & Chalder, 2010). Craske and Barlow (2006) added to the CBT protocol developed by Blanchard et al., (1992) the use of exposure techniques, attentional control exercises and information about the relationship between brain/gut as well as cognitive restructuring to reduce symptom hypervigilance and gastrointestinal anxiety (also termed "visceral anxiety"). The importance of cognitions and behaviors in maintaining symptoms is recognized across CBT protocols, but little research has been conducted into the differential role these may have across the IBS subtypes. Each subtype has a unique set of symptoms (Fehnel et al., 2017; Marquis et al., 2014) associated with specific perceptual experiences (Rønnevig, Vandvik, & Bergbom, 2009). For example, diarrhea is associated with urgency and unpredictability (Drossman et al., 2009; Drossman et al., 2011; Håkanson, 2014; Rønnevig et al., 2009), while constipation may be associated with straining (Håkanson, 2014; Rønnevig et al., 2009).

Understanding whether subtypes have different affective, cognitive and/or behavioral responses may be important for informing therapeutic assessments and formulations as well as better targeting of therapies to optimize outcomes (Drake, Cimpean, & Torrey, 2009; Hamburg & Collins, 2010; Mönnikes, 2011).

There have only been four studies to our knowledge that have assessed associations between cognitions and IBS subtypes (Sugaya & Nomura, 2008; Stengel et al., 2010; Thijssen et al., 2010; Windgassen, Moss-Morris, Goldsmith, & Chalder, in press). Only one of these studies indicated a difference in cognitions between subtypes in that those with IBS-D had higher levels of unhelpful cognitions than those with IBS-C (Windgassen et al., in press). The difference was not significant however and the analysis was limited by power constraints.

Two studies have examined differences in behavioral responses (Katsinelos et al., 2009; Windgassen et al., in press). Windgassen et al (in press) assessed IBS-specific behavioral responses and found that those with IBS-D and IBS-A had higher levels of avoidance behavior than those with IBS-C. Those with IBS-A also had higher levels of safety behaviors than IBS-C and IBS-D. The other study assessing behavioral differences across IBS subtypes found that those with IBS-A had a higher tendency to seek healthcare compared to IBS-C and IBS-D (Katsinelos et al., 2009).

Despite a number of studies examining the association between affective factors and subtypes, the results are inconclusive (Eriksson, Andren, Eriksson, & Kurlberg, 2008; Farnam, Somi, Sarami, Farhang, & Yasrebinia, 2007; Fond et al., 2014; Kibune-Nagasako, Garcia-Montes, Silva-Lorena, & Aparecida-Mesquita, 2016; Muscatello et al., 2010; Prior, Maxton, & Whorwell, 1990; Rey de Castro, Miller, Carruthers, & Whorwell, 2015). However, some studies have suggested that the IBS-A (also referred to as IBS-M for "mixed IBS") subtype may be a particularly burdensome one (Kibune-Nagasako et al., 2016; Singh et al., 2015; Tillisch et al., 2005). Those with IBS-A have been found to have increased anxiety (Kibune-Nagasako et al., 2016) higher levels of symptom severity and somatization compared to those with IBS-C and IBS-D (Tillisch et al., 2005). They have also been found to have worse quality of life and impairment of relationships than those with IBS-C (Singh et al., 2015).

Most of the previous studies assessing differences between IBS subtypes had small samples sizes limiting power to detect significant findings (Eriksson et al., 2008; Katsinelos et al., 2009; Prior et al., 1990; Smiren et al., 2001; Stengel et al., 2010). Furthermore, inconsistency in findings across studies is likely to be the result of the different criteria used to classify bowel subtypes. Many of the studies were

conducted prior to the development of the Rome III criteria, which substantially altered the parameters for assigning bowel subtype classification when compared to Rome II (Ersryd, Posserud, Abrahamsson, & Simren, 2007). Although the Rome IV criteria are now in use, they are similar to Rome III in terms of classification of bowel pattern subtypes (Drossman, 2016).

Aims

This study aimed to assess (1) whether psychological factors implicated in the cognitive behavioral model of IBS were differentially associated with bowel pattern subtypes (2) whether the IBS subtypes, classified according to the Rome III criteria differed in the degree of symptom severity, work and social adjustment, anxiety and depression. Given the limited literature regarding differences in psychological factors, symptom severity and quality of life/impaired functioning between IBS subtypes, this study adds novel and valuable data to previous work with a larger sample size and greater power. We used the validated Rome III criteria to do this. As Rome IV explicitly states that bowel subtypes exist on a continuum rather than being distinct groups, we also assessed cognitive and behavioral associations with scaled frequency measures of hard/lumpy and loose/watery stools.

Method

The present study used baseline and screening data collected as part of the Assessing Cognitive Behavioral Therapy in Irritable Bowel (ACTIB) randomizedd controlled trial (RCT) (Everitt et al., 2015). Five hundred and fifty-eight individuals aged 18 and above were recruited from primary and secondary care sites in South London and the South of England. To be included in the trial participants had to meet the Rome III criteria (Drossman, 2006b) for IBS and have a score of >75 on the IBS symptom severity scale (Francis, Morris, & Whorwell, 1997) at screening. To ensure

a sample of refractory IBS participants also had to have been previously offered first-line therapies, with continuing symptoms of 12 months or longer. Participants were excluded if they had a diagnosis of coeliac disease, inflammatory bowel disease (IBD), peptic ulcer or colorectal carcinoma. These were assessed by medical record checks conducted by physicians and subsequently confirmed by self-report with patients. Blood tests were also conducted to screen out the possibility of symptoms being due to IBD, coeliac disease and anaemia. Unexplained rectal bleeding or weight loss also precluded entry to the trial (Everitt et al., 2015). The data for one participant was lost at screening leaving *N*=557 for analysis in the present paper.

Measures

All questionnaires were completed online immediately prior to randomization (baseline) apart from the Rome III criteria. This was assessed earlier during screening.

Rome III criteria

The Rome III criteria assesses IBS symptoms experienced within a 3 month period, with an item that screens for pain attributable to menstrual bleeding. These items are presented in table 1. Item 10 assesses frequency of diarrhea symptoms and item 11 assesses frequency of constipation on a Likert scale of 0-4.

Classification of IBS Bowel Pattern Subtypes

The Rome III criteria (Drossman, 2006b) was used to assign bowel pattern subtypes (Rome IV is now in use, but had not been developed at the time the ACTIB study commenced). Individuals were classified as IBS-D if they had lose/watery stools ≥ 25% (coded as ≥1) of the time and had hard/lumpy stools < 25% of the time. IBS-C was defined as those with lose stools <25% of the time and hard stools ≥25%. IBS-A was categorized as those with both hard and loose stools ≥25% of the time, while IBS-U experienced hard and loose stools <25%.

IBS Symptom Severity Scale (IBS-SSS)

The IBS-SSS (Francis et al., 1997) is a well-validated measure of symptom severity in IBS, measuring the extent of the severity of abdominal and bowel symptoms in terms of frequency and degree of severity individuals currently experience, specified as "the last 10 days or so". The scale is made up of 5 items with a maximum score of 500. IBS severity is classified as mild for scores between 75 and 175, with scores between 76 and 300 indicating moderate severity. A change in score of ≥50 is considered to be clinically meaningful (Francis et al., 1997). Women are advised to ignore distension relating to periods.

Work and Social Adjustment Scale (WSAS)

The WSAS (Mundt, Marks, Shear, & Greist, 2002) measures the extent that participation in five areas of life has been affected by the illness in question, with higher scores indicating a higher impact. The five areas of life measured are social activities, private leisure activities, relationships, home and work. Each is measured by one item, scored on a scale of 0 to 8, with a total possible score of 40 across the five items. Scores of 10 and above indicate substantial functional impairment and scores of 20 and above indicate severe impairment (Mundt et al., 2002). The scale has been demonstrated to be a valid and reliable measure of participation in life ranging from α=0.70 to 0.94.

Hospital and Anxiety Scale: Anxiety and Depression (HADS)

The HADS is a measure of general anxiety and depression with a subscale for each construct (Zigmond & Snaith, 1983). Individuals are asked to consider how they have felt over the last week. Items such as "*I feel tense or wound up*" measure anxiety and items such as "*I feel as if I am slowed down*" measure depression. They are rated on a scale of 0 to 3. Zero indicates strongly disagree and 3 indicates strongly agree.

Each subscale consists of 7 items, with a total possible score of 21. Scores of 0-7 are considered normal, whilst scores of 8-10 indicate mild anxiety/depression, 11-14 indicate moderate anxiety/depression, and 15 – 21 severe anxiety/depression. The scale has been demonstrated to have good reliability and validity (Zigmond & Snaith, 1983).

Cognitive Scale for Functional Bowel Disorders (CS-FBD)

The CS-FBD (Toner et al., 1998) is a measure of gastrointestinal specific cognitions consisting of 31 items rated on a Likert scale from 1 to 7, with higher scores indicating a higher degree of unhelpful GI related cognitions. The total score ranges from 31 to 217 with good reliability (α= .93) and validity (Toner et al., 1998). An example of an item assessing GI specific cognitions is "I cannot function normally when I get bowel symptoms". Participants rate items based on their experiences over the past month.

The Irritable Bowel Syndrome Behavioral Responses Questionnaire (IBS-BRQ)

Behavioral responses to IBS are subdivided into two subscales measuring safety (control) and avoidance behaviors specific to IBS (Reme et al., 2010). An example of an item on the avoidance behavior subscale is "*I avoid exercise when I have stomach* pains". An example safety behavior item is "*I strain when opening my bowels*". The avoidant subscale has 15 items, and the safety subscale has 11 with items rated on a Likert scale of 1 to 7. Higher scores indicate higher levels of unhelpful GI specific behaviors. The overall scale has been shown to have good reliability and validity α=.86 (Reme et al., 2010).

Analysis

Spearman's rank correlations were conducted to assess whether the cognitive and behavioral factors, in addition to affective factors (anxiety and depression), were

significantly correlated with each other and the dependent variables of interest (symptom severity, frequency of constipation and diarrhea and work and social adjustment). Spearman's rank is used with ordinal data (McDonald, 2009) as with the rankings of stool type frequency. Frequency of the respective bowel patterns (hard/lump or loose/watery) were included as dependent variables in hierarchical regressions in addition to symptom severity generally. The correlations indicated multicollinearity and therefore separate hierarchical regression models were run for each explanatory psychological variable of the CBT model (avoidance behavior, control behavior and unhelpful GI cognitions). Each independent variable was included in block one to assess the association with each of the dependent variables. In block 2, additional potential confounding affective and demographic variables were included. These were age, gender, duration of IBS symptoms, anxiety and depression. This was to assess whether the independent variable was still significantly associated with the dependent variables when controlling for the potential confounder. Bonferroni's correction for multiple variables included in the regression adjusted the alpha to .004.

Differences in psychological factors, symptom severity and work and social adjustment between the Rome III classified IBS subtypes were assessed using one-way ANOVAs. Bowel pattern subtype (IBS-A, C or D) was the independent variable. Separate ANOVAs were run for each dependent variable. To ensure the data met the ANOVA assumptions, normal Q-Q plots were used to assess whether the data was normally distributed and boxplots were used to identify whether there were any outliers for each dependent variable. Homogeneity of variances across subtypes was tested using Levene's test statistic. The F-test statistic was used to assess the overall association between IBS subtypes and the dependent variable using Tukey's Honest

Significant Difference (HSD) to evaluate individual comparisons between the subtypes. Differences in categorical demographic variables (gender, marital status and ethnicity) between subtypes were assessed using a Chi Square test of independence.

Power analyses

A priori power calculations for the hierarchical regressions utilized the correlation coefficients between the lowest significant correlated variables, the adjusted p level of .004 and the desired power of 95%. Calculations indicated a minimum sample size of 297 needed for 95% power to detect effect. A priori power calculations for the ANOVAs indicated a required total sample of 390 participants. This was based on 3 groups, with a conservative effect size of 0.2, at the .05 significance level to achieve 95% power.

Results

The total sample (*N*=557) were predominantly white females with an average age of 43 and illness duration of 10 years (table 2).

Correlations

Table 3 shows the correlations of the psychological variables of interest, stool pattern frequency, symptom severity, work and social adjustment. All psychological factors significantly correlated with each other in addition to symptom severity and work and social adjustment. Frequency of loose/watery stools were significantly positively correlated with avoidance and unhelpful GI related cognitions. They were significantly negatively correlated with control behaviors. Frequency of constipation was significantly positively correlated with control behaviors and negatively correlated with avoidance behaviors.

Hard/lumpy stools

Avoidance behaviors were significantly negatively associated with frequency of hard/lumpy stools (β =.-14, p<.001) and remained significant when controlling for covariates (β =.-18, p<.001). Gender was the only significant covariate, indicating that females were significantly more likely than males to have frequent constipation (β =.-19, p<.001). The model explained 7% of the variance in frequency of hard/lumpy stools (table 4). Control behaviors were significantly positively associated with hard/lumpy stool frequency (β =.25, p<.001), indicating that as control behaviors increased, frequency of constipation increased. This association remained significant when controlling for variables in block 2 (β =.26, p<.001) and explained 9% of the variance in hard/lumpy stool frequency. Unhelpful GI related cognitions were not significantly associated with this stool pattern.

Loose/watery stools

Avoidance behavior (β =.29, p<.001) and unhelpful GI related cognitions (β =.23, p<.001) were significantly positively associated with frequency of loose/watery stools when controlling for potential confounding variables in block 2. No other affective or demographic variables were significantly associated. Avoidant behavior and covariates accounted for 9% of the variation in loose/watery stool frequency and unhelpful GI related cognitions accounted for 6% (table 4). Control behavior was not significantly associated with loose/watery stools.

Symptom Severity

Avoidance behavior was significantly associated with symptom severity (β =.28, p<.001) when assessed in block 2. Increased depression was significantly associated with higher symptom severity (β =.14, p=.004) as was younger age (β = -.15, p<.001). This model accounted for 18% of variance in symptom severity. Control behavior and symptom severity were positively significantly associated (β =.26,

p<.001) when controlling for all covariates entered in block 2. Depression and age were again significantly associated with symptom severity (table 4), with the overall model accounting for 17% of variance in symptom severity. Increased levels of GI cognitions were significantly associated with higher levels of symptom severity (β =.44, p<.001) when controlling for covariates in block 2. Depression was not a significant predictor in this model, although age remained significant (β = -.16, p<.001). This model explained 26% of variance in symptom severity.

Differences between Rome III classified IBS bowel pattern subtypes

The division of the bowel pattern subtypes resulted in just 2.8% of the participant sample (*n*=16) being classified as IBS-U. As this was disproportionately low, IBS-U was excluded from the ANOVAs to preserve sensitivity in finding meaningful differences between groups. Those with IBS-U had similar demographic and illness characteristics to the other subtypes. These characteristics and the mean values for each dependent variable in IBS-U are now contained in supplementary appendix 1. Those with IBS-A were the most prevalent 51.4% (*n*=287), followed by those with IBS-D, which constituted 31.9% (*n*=178). Those with IBS-C made up 13.6% of the sample (*n*=76). Table 2 summarizes the demographic and illness characteristics across the three subtypes. The only significant difference between groups on these variables was the proportion of females, which were higher in the IBS-C and IBS-A groups (table 2).

Some of the dependent variables were not normally distributed in the different IBS subtype groups. CS-FBD was mildly negatively skewed in the IBS-A group, while the control subscale of the BRQ had negative kurtosis in the IBS-C group. WSAS had negative kurtosis in all bowel subtype groups. None of the data was severely skewed. As one-way ANOVAs are quite robust to mild deviations from

normality, particularly in large sample sizes, no transformations were made to the data. A number of outliers were identified for all dependent variables apart from symptom severity. These were checked to ensure they were not the result of data entry and measurement error. The most extreme outliers were removed and the analysis was rerun to determine if inclusion of the outliers had substantially changed the results. They did not, so the outliers were included in the final analysis.

Cognitive and behavioral differences between IBS-C and IBS-D

A significant difference between subtypes was found for GI related cognitions $F(2, 538), 3.50, p = .031$. Tukey's HSD post hoc comparisons identified that IBS-C and IBS-D significantly differed (MD = 11.8, p=.026, 95% CI 1.1, 22.5) with IBS-D having significantly higher levels of unhelpful GI related cognitions (table 5). A significant difference between subtypes was also found for avoidance behaviors $F(2, 538), 10.25, p<.001$, with IBS-D showing significantly higher levels of avoidance behaviors than IBS-C (MD = 11.0, p<.001, 95% CI 5.3, 16.7). Those with IBS-A also had significantly higher levels of avoidance behaviors than IBS-C (MD = 7.7, p=.002, 95% CI 2.3, 13.1). Control behaviors significantly differed across groups $F(2, 538), 10.55, p<.001$. Post hoc tests indicated that IBS-C showed significantly higher levels of control behaviors than those with IBS-D (MD = 4.6, p=.004, 95% CI 1.3, 8.0) as did those with IBS-A (MD =4.3, p<.001, 95% CI 2.0, 6.6). Figure 1 depicts how those with IBS-C had higher mean control behaviors than the group average, with a significant contrast between those with IBS-C and IBS-D. Those with IBS-C also had lower levels of avoidance behavior than the group average, whereas those with IBS-D had higher avoidance behaviors than the group average (panel B).

There were no significant differences between IBS subtypes for anxiety, work and social adjustment or IBS symptom severity (table 5).

Discussion

This paper aimed to assess whether psychological factors identified in the CBT model of IBS were differentially associated with bowel pattern subtypes in IBS. Results indicated that higher levels of control behavior were associated with a higher frequency of hard/lumpy stools (indicative of constipation predominant IBS). Lower levels of avoidance behavior were significantly associated with higher frequency of hard/lumpy stools indicating that individuals with IBS who primarily experienced constipation were less likely to engage in avoidant behaviors. Conversely higher levels of avoidance behavior were associated with higher frequency of loose/watery stools (indicative of diarrhea predominant IBS), as were higher levels of unhelpful GI related cognitions. Avoidance behavior, control behavior and unhelpful GI cognitions were all significantly associated with overall symptom severity. This is congruent with the CBT model of IBS, which suggests that these are interacting factors that contribute to the maintenance of symptoms.

The assessment of differences between the Rome III classified IBS bowel pattern subtypes demonstrated that those with IBS-D were more avoidant than those with IBS-C, whilst those with IBS-C had higher levels of control behaviors than those with IBS-D. Those with IBS-A engaged in both avoidance and control behaviors. Unhelpful GI related cognitions were highest in those with IBS-D and lowest in those with IBS-C.

The findings that increased avoidance behavior was associated with increased frequency of diarrhea symptoms and that individuals with both IBS-A and IBS-D have higher avoidant tendencies than those with IBS-C suggest that treatment techniques may be tailored for these subtypes in IBS. Techniques could target specific reduction of avoidance behaviors rather than control behaviors. A recently developed

CBT-based approach called cognitive behavioral interceptive exposure (CBT-IE) has a predominant focus on the use of exposure techniques to target avoidance in order to reduce symptom severity in IBS (Craske et al., 2011). Strategies used in this treatment may therefore be particularly targeted to those with IBS-D.

The present analysis was cross-sectional and the direction of the relationship between avoidance and symptoms of diarrhea cannot be inferred. The CBT model suggests that the relationship between cognitive and behavioral processes and symptoms are interrelated and cyclical. As such, symptoms of diarrhea may be driving avoidance behavior due to the sense of urgency or lack of control that accompanies them (Kenwright, McDonald, Talbot, & Janjua, 2017). Alternatively, avoidance behavior may serve to increase attention on symptoms and exacerbate them. Previous research has found a significant association between bowel control anxiety and avoidance (Kamboj et al., 2015), which could partly explain the present findings. Avoidance may be driven by anxiety about loosing control of the bowels.

The increased level of unhelpful GI related thoughts in those predominantly experiencing diarrhea symptoms does suggest that CBT treatment and/or the physician consultation may be tailored for this particular IBS subtype. In consultations this may involve eliciting some of the unhelpful thoughts individuals may be having about symptoms and facilitating discussion around symptom management. In CBT, cognitive restructuring techniques may be specifically focussed on IBS-D related thoughts that may be catastrophic (e.g. *"I will have an accident"*).

Interestingly, those with IBS-A appeared to have "the worst of both worlds" in terms of having significantly higher levels of avoidance behavior than those with IBS-C (along with IBS-D) and significantly higher levels of control behavior than those with IBS-D (along with IBS-C). Previous literature has demonstrated an increased

burden in those with IBS-A (Kibune-Nagasako et al., 2016; Singh et al., 2015; Tillisch et al., 2005). This suggests that this subtype has a particular set of challenges in managing fluctuating symptoms and patients may require a more complex, nuanced treatment.

Those with IBS-C had the highest level of control behaviors compared to the other subtypes and overall sample average. Control behaviors included straining on the toilet, checking for blood in stools or wiping excessively. Interestingly, a higher frequency of hard/lumpy stools was negatively associated with avoidance behaviors suggesting that avoidance is not an issue for those with IBS-C.

Females were found to be significantly more likely to have constipation compared to males, in line with previous research (Lovell & Ford, 2012). Females with constipation could benefit from a tailored treatment which focuses on the reduction of control behaviors specifically. It is of course important to consider that in some situations, safety behaviors (avoidance and control) may actually facilitate engagement with everyday activities (Levy & Radomsky, 2014; Rachman, Radomsky, & Shafran, 2008). As with all psychological treatments the individual tailoring of the therapy in keeping with patients own values and goals is imperative.

Informing Practice

Overall avoidance and control behaviors and unhelpful GI related cognitions were found to be significantly associated with symptom severity. This provides support for the CBT model of IBS (Hutton, 2005; Kennedy et al., 2005).

Transdiagnostic approaches identify key areas for change shared across different presentations (Holmes et al, 2018). The goal of personalized treatment is to optimize treatment response by tailoring intervention to individual characteristics and/or mechanisms. It has previously been argued that transdiagnostic approaches

need flexibility to accommodate specific responses within conditions (Chalder & Willis, 2017). The present findings demonstrate ways that this is important in CBT for IBS subtypes. For example, individuals experiencing IBS-D may benefit from techniques focussing on addressing unhelpful cognitions as identified in the CS-FBD. Those with IBS-D and IBS-A may benefit from behavioral strategies targeting avoidance behaviors. In addition, techniques targeting a reduction in control behaviors may be particularly helpful for individuals with IBS-C and IBS-A. The importance of changing IBS specific cognitions and behaviors in IBS has previously been indicated (Windgassen, Moss-Morris, Goldsmith & Chalder, 2017). Future studies could utilize moderated mediation analysis to assess whether bowel pattern subtypes affect treatment mechanisms. This would indicate if and how transdiagnostic CBT treatments could benefit from further adaptation according to subtypes in IBS.

Physicians consulting with IBS patients could also provide brief advice according to symptom subtypes. The provision of psycho-education regarding the role of avoidance and/or control behaviors in the maintenance of symptoms could benefit patients at an early stage of illness presentation. Previous research has suggested that early intervention may be particularly effective by interrupting the formation of negative early illness representations in IBS (Rutter & Rutter, 2007). For example, patients who are newly experiencing symptoms of urgency could be helpfully advised by the GP to minimize symptom related avoidance as this is likely to perpetuate the problem.

The distinction between IBS-C and IBS-D in the behavioral patterns and levels of unhelpful GI related cognitions supports previous research that has suggested there may be differential physiological mechanisms for symptoms in constipation compared

with diarrhea (Krogsgaard et al., 2013; Palsson, Baggish, Turner, & Whitehead, 2012; Wang et al., 2008).

IBS-A has previously been characterized as being more disruptive than the other subtypes (Kibune-Nagasako et al., 2016; Singh et al., 2015; Tillisch et al., 2005). Although our results partially support this in terms of this subtype having higher levels of both maladaptive behaviors, they did not have worse outcomes with regards to symptom severity, work and social adjustment or anxiety and depression. Indeed, none of the IBS subtypes were found to differ in relation to these outcomes. This is in line with previous findings (Jamali et al., 2012; Mönnikes, 2011; Rey de Castro et al., 2015; Simren, Abrahamsson, Svedlund, & Björnsson, 2001). We might conclude therefore that subtypes are not associated with different levels of symptom severity or psychological comorbidity. However, a previous study assessing subgroups in IBS using cluster analysis, found that whilst there were distinct bowel pattern subtypes in line with Rome III and IV criteria, they were further divided into those with high and low psychological and somatic comorbidity subgroups (e.g. IBS-A high comorbidity, IBS-A low comorbidity, etc.). Subgroups with higher rates of comorbidities were associated with higher levels of symptom severity (Polster et al., 2017). It may be of more value therefore to investigate the difference in outcomes between subgroups more comprehensively, defined by several factors simultaneously including psychological comorbidity. (Polster et al., 2017).

Limitations

The extent to which distinctions found between subtypes in cognitive and behavioral measures can be attributed to measurement bias is unclear. This uncertainty arises because some items of the CS-FBD relate more specifically to individuals with IBS-D than those with IBS-C. For example, items such as "*I often*

worry that there may not be a bathroom when I need one" would not be relevant to individuals experiencing constipation. The possibility of measurement bias nevertheless highlights the importance of developing measures that account for the experience of each bowel subtype in IBS. This is increasingly recognized amongst researchers and collaborative working groups in IBS with regards to outcome measures (Fehnel et al., 2017). Our findings suggest that this is important also for psychological and process measures developed for IBS.

Due to the stark contrast in behavioral associations between IBS-D and IBS-C we investigated whether the findings were due to measurement bias, supposing that the number of safety and avoidance subscale items could have been weighted towards the respective bowel pattern subtypes. For instance, the item "*I often go to the toilet and do not pass anything*" (item 7 of the BRQ) may only be applicable to those with constipation. However, inspection of the subscale items showed that there were an equivalent number of safety items related to both types of symptoms.

All analyses were cross-sectional limiting interpretations regarding causality. Furthermore, measurements used specified different periods upon which to form ratings (varying from the last week to last month or no specification at all). Although it is expected that participants generally scored items across the different questionnaires in a way that was representative of their experience within a comparable timeframe this cannot be guaranteed. Future studies should ensure this is standardized. A difficulty with investigating the role of bowel pattern subtypes in IBS is that bowel subtypes have been demonstrated to fluctuate and change (Palsson et al., 2012). As such it is not clear whether the associations found in the present paper would remain consistent with any fluctuations in bowel pattern over-time. Furthermore, the Rome III criteria in the present study was measured at a timepoint

prior to the psychological variables. The time between the assessment of the Rome criteria and the rest of the measures was not standardized across participants as it was collected prior to randomization. This may have confounded the analysis as bowel patterns could have changed by the time the psychological assessments were conducted. Future studies should ensure that subtype assessment is conducted at the same time as the other measures.

Different versions of the Rome criteria differentially classify the subtypes (Drossman, 2006a). The present study used the Rome III criteria to categorize subtypes which are concurrent with the Rome IV classifications (Drossman, 2016). However, the Rome IV states that subtypes are to be based on symptomatic stools only. This is likely to substantially shift the prevalence of each type of subtype.

Research has shown that the menstrual cycle affects the reporting of somatic symptoms and pain in females with IBS (Heitkemper et al., 2003; Riley, Robinson, Wise & Price, 1999). We did not assess the menstrual cycle in this study. Future studies should collect data on this potential confound.

The sample of participants used in the present study had refractory IBS. The associations between psychological factors and bowel patterns subtypes therefore may not be extended to a non-refractory IBS patient population. Tailoring of treatment strategies based on bowel pattern subtypes may therefore differ depending on whether patients were refractory or non-refractory.

Future research should seek to assess bowel pattern associations in a non-refractory population. The participants included in this study were also prepared to enter a CBT trial, which limits generalization to the wider population of individuals with IBS.

Given the potential for measurement bias, the results highlight the importance of developing psychological measures for the different IBS subtypes. Recent

developments in IBS subtype specific outcome measures demonstrates the importance and utility of tailoring such measures (Fehnel et al., 2017). Furthermore, a qualitative study could explore specific motivations for behavioral responses to particular symptoms.

Finally, the present study supports the need for more comprehensively classified subgroups in IBS including psychological as well as clinical factors (Polster et al., 2017; Whitehead et al., 2002). Taking account of the dimensionality of subgroups might also provide a better understanding of the heterogeneous nature of IBS.

Conclusion

The present paper demonstrated that although subtypes did not differ in terms of levels of symptom severity or distress, there were distinct cognitive and behavioral responses between groups. The results provide some direction in the personalization of existing CBT treatments for IBS subtypes. Cognitive and behavioral responses may also be important for inclusion in more multidimensional characterization of diagnostic subgroups in IBS.

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Table*1: Rome III criteria items*

Item	0 Never or rarely	1 Sometimes	2 Often	3 Most of the time	4 Always
1. In the last 3 months, how often did you have discomfort or pain anywhere in your abdomen?					
2. For women: Did this discomfort or pain occur only during your menstrual bleeding and not at other times?	0. No 1. Yes 2. Does not apply because I have had the change of life (menopause) or I am a male				
3. Have you had this discomfort or pain 6 months or longer?	0. Yes 1. No				
4. How often did this discomfort or pain get better or stop after you had a bowel movement?					
5. When this discomfort or pain started, did you have less frequent bowel movements?					
6. When this discomfort or pain started, were your stools (bowel movements) looser?					
7. When this discomfort or pain started how often did you have harder stools?					
8. In the last 3 months, how often did you have hard or lumpy stools?					
9. In the last 3 months, how often did you have loose, mushy or watery stools?					

***Table 2**: Demographics across bowel subtype groups*

	IBS-C ***n* = 76**	**IBS-D** ***n* = 178**	**IBS-A** ***n* = 287**	**F/χ^2**	**P value**
Age at randomization Mean (SD)	45 (12)	43 (13)	42 (12)	1.6	.297
Female gender *n* (%)	64 (84)	116 (65)	230 (80)		<.001
Ethnicity *n* (%)				*1.6*	.454
White	69 (91)	165 (93)	256 (89)		
Other	7 (14)	13 (11)	31 (11)		
Marital Status *n* (%)				*7.3*	.119
Single	18 (24)	37 (21)	90 (31)		
Married/Cohabiting	51 (67)	122 (69)	176 (61)		
Widowed/separated/divorced	7 (9)	19 (11)	21 (7)		
IBS duration mean *n* (SD) in years	10 (8)	10 (9)	11 (10)	0.2	.801

SD = standard deviation, χ^2 *in italics*

Table 3: *Correlations between stool type and psychological factors and measures of severity*

	1	**2**	**3**	**4**	**5**	**6**	7	8
1. Hard/lumpy								
2. Loose watery	-.513**							
3. Control behaviors	.263**	-.089*						
4. Avoidance behaviors	-.128**	.249**	.465**					
5. Unhelpful cognitions	-.045	.182**	.456**	.709**				
6. Anxiety	.061	.029	.278**	.296**	.413**			
7. Depression	.020	-.036	.279**	.293**	.367**	.523**		
8. Work and social adjustment	-.044	.096*	.335**	.548**	.565**	.294**	.430**	
9. Symptom severity	.051	.074	.355**	.357**	.481**	.244**	.252**	.487**

* significant at the .05 level
* significant at the .001 level

Table 4: *Hierarchical regression models*

Dependent Variable	Hard/Lumpy Stools				Loose/Watery Stools				Symptom Severity			
	B	**S.E. *B***	**β**	**P Value**	***B***	**S.E. *B***	**β**	**P Value**	***B***	**S.E. *B***	**β**	**P Value**
(1) Avoidance Behavior												
Constant	1.60	.15			1.01	.17			167.14	11.36		
Avoidance Behavior	-.009	.003	-.14	<.001*	.02	.00	.25	<.001*	1.91	.21	.36	<.001*
	R^2 =.02, F(1,555) =10.8, p<.001				R^2 = .06, F(1,555) =36.9, p<.001				R^2 =.13, F(1,555) = 83.6, p<.001			
(2) Affective and demographic factors												
Constant	1.62	.26			1.27	.31			203.99	20.57		
Avoidance Behavior	-.01	.003	-.18	<.001*	.02	.003	.29	<.001*	1.47	.22	.28	<.001*
Anxiety	.01	.01	.04	.42	-.01	.02	-.03	.54	1.11	1.11	.05	.32
Depression	.02	.02	.07	.19	-.04	.02	-.12	.02	3.63	1.26	.14	.004*
Age	-.001	.004	-.02	.75	-.003	.01	-.03	.48	-1.08	.32	-.15	.001*
IBS duration	.004	.005	.04	.44	.001	.01	.01	.82	.18	.42	.02	.67
Gender	-.51	.11	-.19	<.001*	.25	.13	.08	.06	-8.19	8.87	-.04	.36
	Δ R^2 =.05, F(6,550) =6.4, p<.001				**Δ** R^2 =.02, F(6,550) =14.6, p<.001				**Δ** R^2 =.04, F(6,550) =19.4, p<.001			
	Total R^2 =.07				Total R^2 =.09				Total R^2 =.18			
(1) Control Behavior												
Constant	-.13	.21			2.46	.26			120.82	17.03		
Control Behavior	.03	.004	.25	<.001*	-.01	.01	-.08	.05	3.11	.36	.35	<.001*
	R^2 =.06, F(1, 555) = 37.8, p<.001				R^2 =.01, F(1, 555) = 3.9, p=.05				R^2 =.12, F(1, 555) = 75.5, p<.001			
(2) Affective and demographic factors												
Constant	-.19	.31			2.81	.38			164.42	24.95		
Control Behavior	.03	.005	.26	<.001*	-.01	.01	-.09	.06	2.36	.38	.26	<.001*
Anxiety	-.004	.01	-.01	.78	.01	.02	.02	.65	1.43	1.11	.06	.20
Depression	-.01	.01	-.04	.45	-.01	.02	-.03	.58	3.66	1.27	.14	.004*
Age	.005	.004	.06	.23	-.01	.01	-.09	.05	-1.08	.32	-.15	.001*
IBS duration	.003	.005	.03	.52	.002	.01	.02	.73	.19	.42	.02	.66
Gender	-.40	.11	-.15	<.001*	.19	.14	.06	.17	-.99	9.02	-.004	.91
	Δ R^2 =.03, F(6, 550) = 9.5, p=.003				**Δ** R^2 =.01, F(6, 550) = 7.0, p=.09				**Δ** R^2 =.05, F(6,550) = 18.4, p<.001			
	Total R^2 =.09				Total R^2 =.02				Total R^2 =.17			
(1) Unhelpful cognitions												
Constant	1.48	.22			.94	.26			58.89	16.33		
Unhelpful Cognitions	-.002	.001	-.07	.12	.01	.002	.17	<.001*	1.37	.11	.48	.001*
	R^2 =.004, F(1,555) = 2.4, p=.12				R^2 =.01, F(1, 555) = 16.7, p<.001				R^2 =.23, F(1,555) = 167.33, p<.001			
(2) Affective and demographic factors												
Constant	1.61	.31			.94	.26			117.76	24.46		
Unhelpful Cognitions	-.004	.002	-.12	.01	.01	.002	.23	<.001*	1.24	.12	.44	.001*
Anxiety	.01	.02	.05	.38	-.02	.02	-.05	.36	-.59	1.07	-.03	.58

Depression	.02	.02	.05	.30	-.04	.02	-.11	.04	2.59	1.20	.10	.03
	B	**S.E. *B***	**β**	**P Value**	***B***	**S.E. *B***	**β**	**P Value**	***B***	**S.E. *B***	**β**	**P Value**
Age	.00	.004	.002	.96	-.01	.01	-.06	.21	-1.13	.30	-.16	<.001*
IBS duration	.004	.005	.03	.47	.002	.01	-.01	.78	.18	.40	.02	.64
Gender	-.52	.12	-.19	<.001*	.27	.13	.09	.04	-3.85	8.44	-.02	.65
	Δ R^2 =.05, F(6,550), 6.1, p<.001 Total R^2 =.05				**Δ** R^2 =.03, F(6, 550), 5.3, p<.001 Total R^2 =.06				**Δ** R^2 =.03, F(6, 550), 31.64, p<.001 Total R^2 =.26			

Table 5: *Mean differences in psychological outcomes between IBS subtypes*

	F	P_1	Group Contrast	Mean Difference	P_2	95% CIs Lower Limit	95% CIs Upper Limit
Symptom Severity	1.7	.19	IBS-C – IBS-D	-6.1	.26	-15.2	3.0
			IBS-C – IBS-A	-1.9	.86	-10.5	6.6
			IBS-A – IBS-D	-4.2	.27	-2.2	10.5
Work and Social Functioning	0.6	.58	IBS-C – IBS-D	-0.8	.79	-3.5	2.0
			IBS-C – IBS-A	0.1	>.99	-2.5	2.7
			IBS-A – IBS-D	-0.8	.56	-1.1	2.7
Cognitions	3.5	.031	IBS-C – IBS-D	-11.8	.026	-22.5	-1.1
			IBS-C – IBS-A	-9.8	.060	-19.8	0.3
			IBS-A – IBS-D	-2.0	.80	-5.4	9.5
Avoidance Behaviors	10.3	<.001	IBS-C – IBS-D	-11.0	<.001	-16.7	-5.3
			IBS-C – IBS-A	-7.7	.002	-13.1	-2.3
			IBS-A – IBS-D	-3.3	.13	-0.7	-7.3
Safety / control Behaviors	10.4[a]	<.001	IBS-C – IBS-D	4.6	.004	1.3	8.0
			IBS-C – IBS-A	0.3	.97	-2.8	3.5
			IBS-A – IBS-D	4.3	<.001	2.0	6.6
Anxiety	.8	.43	IBS-C – IBS-D	0.7	.41	-0.6	2.1
			IBS-C – IBS-A	0.6	.50	-0.7	1.9
			IBS-A – IBS-D	0.1	.95	-0.8	1.1
Depression	1.3	.27	IBS-C – IBS-D	0.7	.33	-0.5	1.9
			IBS-C – IBS-A	0.7	.26	-0.4	1.9
			IBS-A – IBS-D	-0.03	>.99	-0.9	0.8

F, F statistic; [a], Welch statistic; P_1, significance of one way ANOVA between groups at 0.05 level; P_2, significance of one way ANOVA post hoc comparisons at standard significance level 0.05; CIs, confidence intervals

0

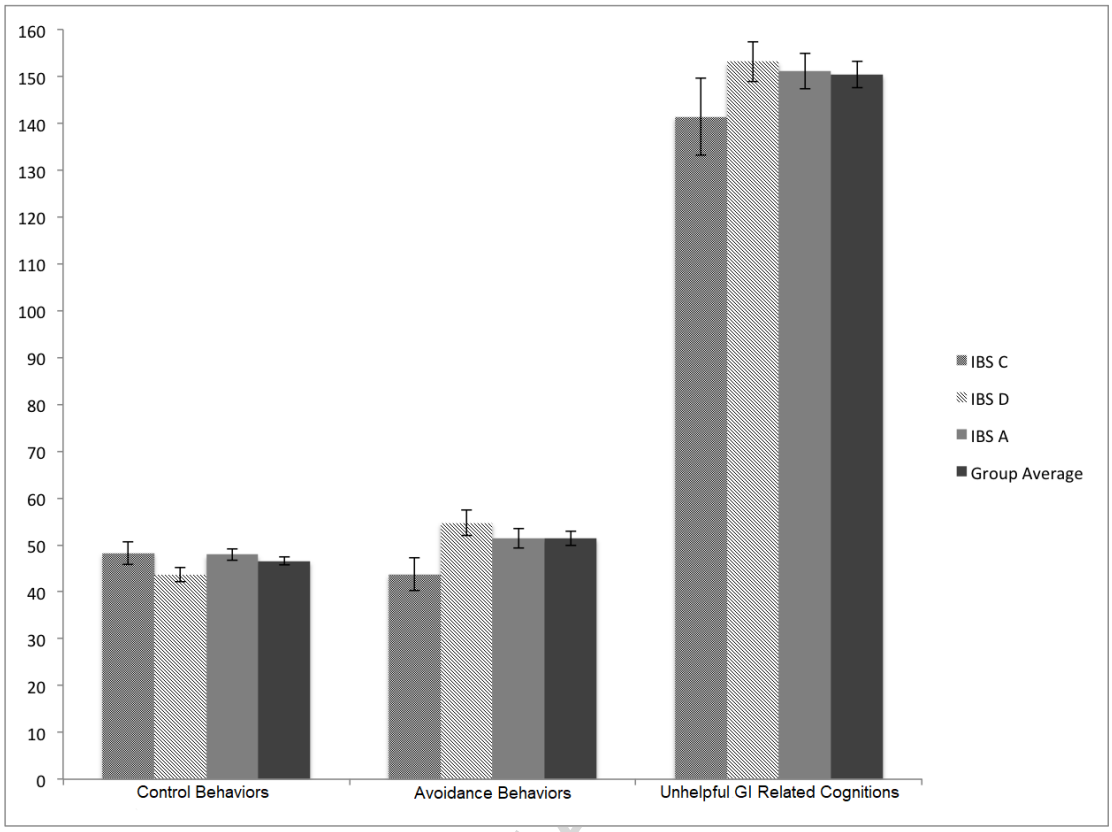

Figure 1: Differences in control behavior, avoidance behavior and unhelpful GI related cognitions between Rome III bowel subtypes compared against total group average

Highlights

- Behavioral responses to symptoms are different across the IBS subtypes
- Avoidance behaviors are higher in diarrhea predominant IBS
- Control behaviors are higher in constipation predominant IBS
- Those with alternating IBS engage in both avoidance and control behaviors
- Gastrointestinal related cognitions are higher in diarrhea predominant IBS