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Key mechanisms of cognitive behavioural therapy in irritable bowel syndrome: the importance of gastrointestinal related cognitions, behaviours and general anxiety

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Abstract

Background: Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterised by abdominal pain and altered bowel movements. Cognitive behavioural therapy (CBT) has been shown to be effective in reducing symptom severity in IBS and enhancing quality of life/ functioning. The present study sought to identify how CBT achieves change in these outcomes.

Method:

Secondary analysis was conducted on 149 patients with irritable bowel syndrome who had been randomised to cognitive behavioural therapy plus an antispasmodic medication or antispasmodic alone. Single and sequential mediation was modelled using structural equation modelling. Gastrointestinal (GI) related avoidance behaviour, safety behaviour, cognitions and general anxiety were included as mediators.

Results:

GI safety behaviours, cognitions and general anxiety mediated treatment effect on the outcomes of symptom severity and work and social adjustment. Avoidance behaviour was not a significant mediator for either outcome. Sequential mediation models indicated that unhelpful GI related cognitions reduced before anxiety did, and this sequential path (R → GI related cognitions → anxiety → outcome) was significant for both symptom severity ($b=0.22$, CI [-0.40 to -0.90], $p=.005$) and work and social adjustment ($b=.26$, CI [-.44 to -.11], $p=.003$) where ‘R’ is randomisation. Reduction in GI safety behaviours also preceded reduction in anxiety. This sequence (R → GI safety behaviours → anxiety → outcome) was significant for both symptom severity ($b=0.11$, CI [-.24 to -.01], $p=.049$) and work and social adjustment ($b=0.12$, CI [-.23 to -.03], $p=.03$).

Conclusion:

Results suggest that it is important for psychological treatments to target IBS specific factors for change.

Keywords

Cognitive behaviour therapy; irritable bowel syndrome; treatment mechanisms; illness related cognitions; safety behaviours; anxiety
Introduction

Irritable bowel syndrome is a functional gastrointestinal disorder characterised by abdominal pain and associated changes in bowel habits [1]. The prevalence of IBS is estimated to be between 10 and 22% in the UK [2, 3] with a similar global prevalence rate [4]. There are no physiological diagnostic markers for IBS and it has long been established as a ‘biopsychosocial illness’ [5, 6]. As such physiological factors such as genetics or infection interact with psychological and social factors such as unhelpful gastrointestinal (GI) related cognitions, anxiety and life stress to result in bowel symptoms and abdominal pain.

Cognitive behavioural therapy (CBT) has been shown to effectively reduce symptom severity and enhance quality of life in IBS [7-9]. However, there is not one generic CBT model or approach in IBS. A number of CBT models for IBS have been developed [10-12] utilising different cognitive and behavioural strategies to target the key mechanisms identified by the respective models. The three system’s model for IBS, as based on Lang’s three system’s model of panic disorder [13], identifies gastrointestinal (GI) related cognitions and behaviours as key factors in maintaining symptoms [12]. Therapeutic strategies such as challenging unhelpful thinking patterns and goal setting are used to change cognitions and behaviours. More recently, an interoceptive CBT model of IBS (CBT-IE) has been developed [11]. This model posts that symptoms are maintained by GI specific anxiety and hypervigilance to symptoms [11]. Exposure based techniques (interoceptive and in vivo) are used in CBT-IE to reduce GI specific anxiety and hypervigilance.

Identifying Treatment Mechanisms

The term ‘mechanism’ refers to the processes through which treatments have effect on the desired outcome [14]. Understanding what the key mechanisms of treatment are, is important for modifying treatments so that they can more effectively target identified mechanisms of action [15]. This has the potential for improving the efficacy and efficiency of treatments. Insight into mechanisms of change in treatments can also inform the understanding of the nature of IBS. Evidence for key processes in the maintenance of IBS can be inferred from research demonstrating how treatments reduce symptom
severity through change in specific mechanistic processes [14, 16]. I.e. if treatment works by reducing unhelpful GI cognitions we can infer that these cognitions are likely maintaining factors of IBS.

Both three system’s CBT and CBT-IE may be classified as ‘endogenous’ stress models of IBS [17]. Both identify stress-inducing processes arising specifically from IBS symptoms (e.g. GI specific cognitions, behaviours, anxiety) as key maintaining processes of IBS [17, 18]. In contrast ‘exogenous’ stress models of IBS postulate that symptom-exacerbating stress arising from factors external to IBS (e.g. stress or general anxiety), are central maintaining factors of IBS [17]. While there is evidence to show that anxiety exogenous to IBS may have a causal role in the onset [19] and that those with IBS have increased stress reactivity [20, 21], there is less evidence suggesting that changing such exogenous factors precede change in IBS symptoms [16]. A systematic review of treatment mechanisms in CBT for IBS suggested that across different CBT treatment protocols change in IBS-specific processes, particularly GI related cognitions, were key in reducing symptom severity and improving quality of life (QoL) [16].

Cognitive and behavioural responses have been shown to have a mechanistic role in treatment effect across CBT protocols [17, 22-25]. In CBT-IE, avoidance was shown to mediate the a reduction of symptom severity [25]. Similarly, the mechanistic role of both GI related cognitions and behaviours was demonstrated in a randomised controlled trial assessing the efficacy of a three system’s CBT treatment when added to an antispasmodic versus an antispasmodic alone [22]. The data from this trial is used in the present paper. The trial recruited adults from primary and secondary care sites in South London and assessed outcomes at baseline, 1.5, 3, 6 and 12 months post-randomisation [12]. CBT plus antispasmodic medication were superior to medication alone in reducing symptom severity and improving functioning at 1.5 and 3 months follow-up [12, 26]. There was some waning of response at 6 and 12 months. The trajectories for both outcomes are illustrated in panel A and B in appendix C.

Previous mediation analysis using this data conducted sequential modelling in order to identify whether GI related cognitions or behaviours changed first in a sequence of change from treatment to the outcomes of symptom severity, work and social adjustment and anxiety [22]. Separate models were run for each outcome and GI related behaviours were assessed as one construct that included
both avoidance behaviours (e.g. avoiding foods or situations) and safety behaviours (e.g. checking stools or access to the toilet). Change in behaviour was found to precede change in cognitions for all outcomes. However, the analysis did not include mediators measured at consecutive time points, limiting inferences about causality.

The present study sought to build on the previous study and wider research to explore in more detail the order of change during therapy. Based on the endogenous models of IBS, it is hypothesized that for change in outcomes to occur, it is primarily important for GI related cognitions and behaviours to change. Change in these IBS specific processes is hypothesized to lead to reduction in general anxiety. In contrast, exogenous models would lead us to expect that general anxiety would change prior to GI related cognitive and behavioural processes, as general anxiety (or stress) is the key target for change in such treatment approaches.

The present analyses advances the analytic strategy used previously by using consecutive time points (from baseline to 12 months) to aid inferences about causality. Although the significant treatment by group effect was lost by 6 months, it has been argued that it is important to conduct mechanistic research in the absence of significant treatment effects. This allows information to be gathered about what may have been responsible for this the lack of sustained effect. For example, whether the treatment did not target the treatment mechanisms as expected [27, 28]. Given that a previous factor analysis found two factors, namely control or safety behaviours and avoidance behaviour were distinguishable, we also wanted to explore these potential mediators separately [29]. The aims of the present study were to (1) identify whether CBT produced change in symptom severity and work and social adjustment via a change in anxiety, cognitions, avoidance behaviours and/or safety behaviours (2) identify whether mediating effects found in cognitions and/or behaviours preceded or were preceded by change in anxiety to produce change in outcomes.
Figure 1: Mediation models tested. Anx, anxiety; Cog, GI related cognitions; Beh A, GI avoidance behaviour; Beh S, GI safety behaviour; M1, first mediator in sequence; M2, second mediator in sequence; O, outcome; R, randomisation. Models 1-4 depict simple mediation models tested. The full mediation model does not identify a direct relationship between the randomisation factor (treatment) and outcome and the partial mediation model does. Full and partial mediation models were conducted for each sequential mediation model tested. In each mediation model, baseline measures of the outcome and mediators were controlled for.

Method

Design
The present study is a secondary mediation analysis of an RCT comparing the effect of CBT plus Mebeverine with Mebeverine alone on symptom severity and WSA outcomes [12, 26]. Results indicated that the addition of CBT to mebeverine improved symptom severity and work and social adjustment up to three months after treatment compared to mebeverine alone.

**Participants and procedure**

Individuals aged between 16 and 50, diagnosed with IBS and meeting the Rome I diagnostic criteria of IBS were recruited from London general practices. A total of 149 participants were randomised to either receive mebeverine alone or to receive CBT in addition to mebeverine [12]. Data of one participant were completely missing, leaving 148 participants for inclusion in the mediation analysis.

**CBT treatment**

A CBT treatment based on Lang’s three systems model [13] was developed for IBS (appendix A). The treatment included psycho-education, cognitive restructuring and behavioural techniques [12]. Psycho-education provided information about the physiology of the bowel and the brain-gut connection. Cognitive restructuring was aimed at making individuals aware of unhelpful GI-related thoughts, recognising how these affected their behaviours, and GI symptoms. Behavioural techniques involved goal setting to increase helpful behaviours such as eating regular meals, whilst reducing unhelpful behaviours. These could be avoidance behaviours such as avoiding situations that may be impacted by bowel symptoms, or safety behaviours such as taking precautionary measures like trying to force the bowels to empty before leaving the house. Techniques to manage stress and prevent relapse were also included.

**Measures**

**Primary Outcomes**

The *IBS Symptom Severity Scale (IBS-SSS)* measures symptom severity specific to IBS, and has been found to be sensitive to change over time [30]. The maximum score is 500, with scores <75 indicating
normal bowel function. Scores between 75-174 indicate mild IBS, 175-299 moderate IBS and scores between 300-500 indicate severe IBS. The scale has been shown to have good reliability and validity [30].

The Work and Social Adjustment Scale [31] is a validated measure of work and social adjustment (WSA)/functioning. It contains 5 items each rated 0 - 8, with a total potential score of 40. The items assess individuals’ ability to engage in day-to-day tasks at work, at home, socially, with family and in relationships. It was found to be a reliable and valid measure of impaired functioning [31].

Mediators

The Cognitive Scale for Functional Bowel Disorders (CSFBD) [32] is a measure of GI related cognitions. An example questionnaire item is “my bowel symptoms make me feel out of control”. The scale consists of 25 items, with a possible total score of 25 to 175 with higher scores indicating more illness-related cognitions. The measure has been demonstrated to have good reliability and validity [32].

The Hospital Anxiety and Depression Scale (HADS) [33] is a general measure of depression and anxiety. Just the anxiety subscale was used to assess general anxiety with items such as “I feel tense or wound up”. This is made up of 7 items scored from 0 to 3, with a total possible score of 21. Scores of 8 and above are said to indicate anxiety [34] with good sensitivity (0.9).

The IBS Behavioural Responses Questionnaire (IBS-BRQ) [29] was used to measure GI avoidance behaviour (“I avoid going out in case I have problems with my IBS”) and GI safety behaviour (“I spend more time on the toilet than I would ideally like”). Both types of behaviour are asserted to maintain anxiety in the anxiety and health anxiety literature [35]. However, the nature of each behaviour is different. One seeks to exert control over the experience of illness in some way (safety behaviours) and the other relies on withdrawing from certain activities to prevent anticipated troublesome symptoms or experiences (avoidance behaviours).

Statistical Analysis

General
The data were standardised by subtracting the mean of the given scale from each score and dividing by
the standard deviation for each given time point. Standardising data reduces potential problems of
multicollinearity and allows comparison of indirect effects [36]. Using Z scores in mediation has been
shown to provide more accuracy in statistical tests and confidence limits, as shown in several
stimulation studies [37].

It has been recommended that mediation variables are assessed for significant change prior to
mediation analysis [38]. For anxiety and GI related cognitions, assessment of main effects and
interactions were conducted in the previous mediation paper [12, 26] and presented again in this
paper only for contextual clarity. Repeated measures ANOVAs were then conducted to assess the main
effects of group and time and the interaction (time x group) on the avoidance and safety behavioural
subscales of the BRQ, over the three time points included in the mediation analysis (1.5, 3 and 6
months post randomisation). This analysis allowed assessment of whether change in mediator
variables occurred over time, between the treatment and control groups. Significant interactions
indicate that there was a change over time, which differed between groups

Mediation models

Mediation models were fitted in the structural equation modelling (SEM) framework using Mplus
version 7. SEM is advocated as an approach that allows simultaneous modelling of several variables,
enabling the investigation of more complex mediation models [27, 39, 40] than would be possible by
conducting a series of regressions utilising Baron & Kenny’s framework [41]. Path tracing rules [42] akin
to what is specified in the mediation literature were used to calculate indirect effects [40]. Bias-
corrected bootstrap estimates and confidence intervals were calculated for the indirect effects as
recommended for the sample size [43]. Full information maximum likelihood was used to handle
missing data as utilised by MPlus software and recommended in the literature to reduce bias and
conserve sensitivity of analysis [44].

All mediation models controlled for baseline measures of the mediator and outcome to account for the
potential confounding of the non-randomised mediator-outcome relationship, which is widely agreed
to be important [40, 45, 46]. Baseline measures of the mediator and outcome are likely to be amongst
the most important confounders [47, 48] and may also provide adjustment for other related confounders not included in the model. Baseline data collected just prior to randomisation was included in the analysis for all measures, apart from GI avoidance and safety behaviours as these data were not collected at this timepoint. In these cases, data from when the participants first entered the trial (2 weeks prior to randomisation) was used.

Simple mediation models with single mediators were run first to assess whether the variables identified in the CBT model of IBS significantly mediated treatment effect on outcome (figure 1). Models were run for each potential mediating variable: anxiety, GI related cognitions, GI avoidant and GI safety behaviours. These were run separately for each outcome also.

Sequential mediation models were then run to further elucidate the relationship between cognitive and behavioural processes and anxiety. Specifically, we sought to understand whether it was necessary for cognitive and behavioural change to occur first, to produce a subsequent reduction in anxiety, ultimately leading to improved outcomes. To assess this, we compared models that had cognitive or behavioural change preceding change in anxiety, to models where change in anxiety preceded cognitive or behavioural change.

To allow for causal interpretations of mediational analyses, it is important to ensure that variables are measured in a plausible temporal sequence [40, 46, 49, 50]. In other words, to infer that treatment causes change in a mediator and that this change causes subsequent change in an outcome, the mediator should be measured at an earlier time point than the outcome. To this end, the simple mediation models included mediators measured at 1.5 months post randomisation and outcomes measured at 12 month post randomisation (figure 1). In sequential mediator models, the first mediator in the sequence was measured at 1.5 months post randomisation and the second mediator at 3 months post randomisation. Outcome measures assessed at 12 month post randomisation were also used as this was the ultimate follow up time point and there was no significant difference between outcomes at 6 months and 12 months post randomisation.

Three types of model fit criteria were used to select the best fitting mediation model. Final models were selected based on whether they had acceptable or good fit across the majority of the three types
of fit indices (absolute, incremental and information) as has previously been recommended [51-55],
giving priority to the RMSEA, CFI and TLI. This method was designed to tackle the sometimes conflicting
criteria and the issues with model selection uncertainty [55]. Further details of the analysis are
contained in appendix B.

Results

Participants

The majority of participants met the Rome I diagnostic criteria for irritable bowel syndrome (85%). A
minority of patients had normal bowel function to mild symptoms (10%), with 89 (38%) participants
having moderate symptoms and 122 having severe symptoms (52%). Participants were predominantly
women (82%), white British (65%) with a mean age of 33.8 years (SD 8.6). The mean baseline measures
are presented in table 1 and further detailed elsewhere [12, 26].

Changes in mediating variables: Anxiety, behaviours and cognition

The line graphs in figure 2 depict change in mediator variables over the 3 time points included in the
mediation analysis. The changes in anxiety and cognition were previously reported in detail [12, 26]
with a summary of the results presented here. There was a significant main effect of group but not
time on both anxiety and GI related cognitions, indicating that on average over the different follow-up
time points anxiety and GI related cognitions were significantly lower in the CBT group than in the
control group (figure 2, panels A and B).

Analysis of the behavioural subscales in the present paper found that there was a significant main
effect of group on GI safety behaviours F(1,97) =12.81, p=.001 with lower levels of GI safety behaviours
at follow-up on average in the CBT group. The main effect of time was significant, F(1.62,156.76) =4.47,
p=.02, which is likely due to the relatively large decrease between baseline and post-treatment ratings
of GI safety behaviours in the CBT group. For avoidance behaviours there was no significant main effect
of time F(1.60,154.93) =2.49, p=.10 or group F(1,97) =1.16, p=.29 suggesting that there was no
difference between the groups on average over the three time points. This may be in part due to the
difference between the two groups at baseline, with their profile plots crossing between baseline and post treatment (figure 2, panel C). There were significant group*time interaction effects for all four potential mediator variables (all p < 0.010), which was due to the differences in effects between baseline and the two follow-up measurements.

Table 1: Baseline measures taken at 2 weeks prior to randomisation (n=235)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>Standard deviation</th>
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<tbody>
<tr>
<td>Symptom severity</td>
<td>298.2</td>
<td>94.7</td>
</tr>
<tr>
<td>Work and social adjustment</td>
<td>14.3</td>
<td>8.1</td>
</tr>
<tr>
<td>GI related cognitions</td>
<td>108.4</td>
<td>30.6</td>
</tr>
<tr>
<td>GI related safety behaviours</td>
<td>44.7</td>
<td>10.7</td>
</tr>
<tr>
<td>GI related avoidance behaviours</td>
<td>44.5</td>
<td>17.5</td>
</tr>
<tr>
<td>Anxiety</td>
<td>11.0</td>
<td>4.6</td>
</tr>
<tr>
<td>Depression</td>
<td>7.2</td>
<td>3.8</td>
</tr>
</tbody>
</table>
Figure 2: Change over time in mediator variables anxiety (panel A), GI related cognitions (panel B), avoidance (panel C) and control behaviours (panel D) between groups. 95% confidence intervals plotted for each time point.
<table>
<thead>
<tr>
<th>Model (+ baseline)</th>
<th>RMSEA [90% CI]</th>
<th>CFI</th>
<th>TLI</th>
<th>AIC</th>
<th>BIC</th>
<th>$\chi^2$ GOF</th>
<th>Indirect effect $p$</th>
</tr>
</thead>
</table>

Table 2: Mediation analysis of symptom severity & work and social adjustment scores with

Randomisation (R), Anxiety (A), GI related cognitions (C), GI Safety Behaviours (SB), IBS Symptom Severity Score (IBS-SSS) and Work and Social Adjustment (WSA)
### Basic Mediation Models

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<tbody>
<tr>
<td></td>
<td>R-&gt;A&gt;IBS SSS</td>
<td>0 [0, 0.15]</td>
<td>1.0</td>
<td>1.02</td>
<td>1616.5</td>
<td>1670.5</td>
<td>( \chi^2(2)=1.36, ) ( p=.5 ) .002</td>
</tr>
<tr>
<td></td>
<td>R-&gt;C&gt;IBS SSS</td>
<td>0 [0, 0.06]</td>
<td>1.0</td>
<td>1.05</td>
<td>1538.8</td>
<td>1592.8</td>
<td>( \chi^2(2)=0.18, ) ( p=.92 ) .005</td>
</tr>
<tr>
<td></td>
<td>R-&gt;AB&gt;IBS SSS</td>
<td>0.041 [0, 0.17]</td>
<td>0.996</td>
<td>0.984</td>
<td>1594.8</td>
<td>1648.7</td>
<td>( \chi^2(2)=2.49, ) ( p=.29 ) .19</td>
</tr>
<tr>
<td></td>
<td>R-&gt;SB&gt;IBS SSS</td>
<td>0 [0, 0.15]</td>
<td>1.0</td>
<td>1.01</td>
<td>1616.2</td>
<td>1670.2</td>
<td>( \chi^2(2)=1.62, ) ( p=.45 ) .005</td>
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### Sequential Mediation Models

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<tbody>
<tr>
<td></td>
<td>R-&gt;C&gt;A&gt;IBS SSS*</td>
<td>0.070 [0, 0.14]</td>
<td>0.981</td>
<td>0.952</td>
<td>2111.6</td>
<td>2198.5</td>
<td>( \chi^2(6)=10.38, ) ( p=.1 ) .006</td>
</tr>
<tr>
<td></td>
<td>R-&gt;A&gt;C&gt;IBS SSS*</td>
<td>0.102 [0, 0.17]</td>
<td>0.949</td>
<td>0.872</td>
<td>2174.0</td>
<td>2260.9</td>
<td>( \chi^2(6)=1.50, ) ( p=.59 ) .16</td>
</tr>
<tr>
<td></td>
<td>R-&gt;SB&gt;A&gt;IBS SSS*</td>
<td>0.08 [0, 0.15]</td>
<td>0.976</td>
<td>0.939</td>
<td>2218.9</td>
<td>2305.8</td>
<td>( \chi^2(6)=11.17, ) ( p=.08 ) .049</td>
</tr>
<tr>
<td></td>
<td>R-&gt;A&gt;SB&gt;IBS SSS</td>
<td>0.119 [0.05, 0.19]</td>
<td>0.954</td>
<td>0.862</td>
<td>2200.6</td>
<td>2290.5</td>
<td>( \chi^2(6)=15.14, ) ( p=.008 ) .01</td>
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### Work and Social Adjustment

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<tbody>
<tr>
<td></td>
<td>R-&gt;A&gt;WSA</td>
<td>0.041 [0, 0.14]</td>
<td>0.997</td>
<td>0.988</td>
<td>1543.5</td>
<td>1597.4</td>
<td>( \chi^2(2)=2.49, ) ( p=.29 ) .001</td>
</tr>
<tr>
<td></td>
<td>R-&gt;C&gt;WSA</td>
<td>0.034 [0, 0.17]</td>
<td>0.998</td>
<td>0.993</td>
<td>1393.3</td>
<td>1447.2</td>
<td>( \chi^2(2)=2.34, ) ( p=.31 ) .001</td>
</tr>
<tr>
<td></td>
<td>R-&gt;AB&gt;WSA</td>
<td>0 [0, 0.10]</td>
<td>1.0</td>
<td>1.04</td>
<td>1542.2</td>
<td>1596.1</td>
<td>( \chi^2(2)=0.46, ) ( p=.79 ) .09</td>
</tr>
<tr>
<td></td>
<td>R-&gt;SB&gt;WSA</td>
<td>0 [0, 0.07]</td>
<td>1.0</td>
<td>1.05</td>
<td>1567.1</td>
<td>16120</td>
<td>( \chi^2(2)=0.22, ) ( p=.90 ) .004</td>
</tr>
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### Sequential Mediation Models

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<tr>
<td></td>
<td>R-&gt;C&gt;A&gt;WSA*</td>
<td>0.151 [0.10, 0.21]</td>
<td>0.929</td>
<td>0.822</td>
<td>1974.8</td>
<td>2061.8</td>
<td>( \chi^2(5)=26.20, ) ( p=0.001 ) .002</td>
</tr>
<tr>
<td></td>
<td>R-&gt;A&gt;C&gt;WSA*</td>
<td>0.160 [0.10, 0.22]</td>
<td>0.911</td>
<td>0.777</td>
<td>2018.6</td>
<td>2105.5</td>
<td>( \chi^2(6)=28.63, ) ( p&lt;.001 ) .003</td>
</tr>
<tr>
<td></td>
<td>R-&gt;SB&gt;A&gt;WSA*</td>
<td>0.096 [0.03, 0.16]</td>
<td>0.966</td>
<td>0.914</td>
<td>2146.3</td>
<td>2233.2</td>
<td>( \chi^2(6)=14.18, ) ( p=.03 ) .03</td>
</tr>
<tr>
<td></td>
<td>R-&gt;A&gt;SB&gt;WSA*</td>
<td>0.115 [0.06, 0.15]</td>
<td>0.954</td>
<td>0.884</td>
<td>2125.8</td>
<td>2212.7</td>
<td>( \chi^2(6)=17.66, ) ( p=.007 ) .02</td>
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<tr>
<td>WSA*</td>
<td>0.18</td>
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Rows in bold indicate best fitting model in comparison of two mediation sequences; * denotes full mediation model; RMSEA, root mean square error of approximation; CFI, comparative fit index, TLI, Tucker-Lewis Index; AIC, Akaike’s Information Criterion; BCC, Brown-Cudeck criteria; $\chi^2$ GOF, Chi square goodness of fit.
Table 3: Direct, Indirect & Total Effects in all models

<table>
<thead>
<tr>
<th>Symptom Severity</th>
<th>Work and social adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>b (95% CI)</td>
</tr>
<tr>
<td>R → anxiety → IBS-SSS</td>
<td>R → anxiety → WSA</td>
</tr>
<tr>
<td>Group -&gt; Anxiety</td>
<td>-0.60 (-0.90, -0.30)</td>
</tr>
<tr>
<td>Anxiety -&gt; IBS SSS</td>
<td>0.44 (0.25, 0.62)</td>
</tr>
<tr>
<td>Group -&gt; IBS SSS</td>
<td>-0.04 (-0.33, -0.07)</td>
</tr>
<tr>
<td>Group -&gt; Anxiety -&gt; IBS SSS</td>
<td>-0.13 (-0.46, -0.11)</td>
</tr>
<tr>
<td>R → cognitions → IBS-SSS</td>
<td>R → cognitions → WSA</td>
</tr>
<tr>
<td>Group -&gt; Cognitions</td>
<td>-0.53 (-0.79, -0.26)</td>
</tr>
<tr>
<td>Cognitions -&gt; IBS SSS</td>
<td>0.45 (0.23, 0.66)</td>
</tr>
<tr>
<td>Group -&gt; IBS SSS</td>
<td>-0.08 (-0.37, -0.23)</td>
</tr>
<tr>
<td>Group -&gt; Cognitions -&gt; IBS SSS</td>
<td>-0.24 (-0.43, -0.09)</td>
</tr>
<tr>
<td>R → avoidance behaviour → IBS-SSS</td>
<td>R → avoidance behaviour → WSA</td>
</tr>
<tr>
<td>Group -&gt; Avoidance behaviour</td>
<td>-0.49 (-0.73, -0.23)</td>
</tr>
<tr>
<td>Avoidance behaviour -&gt; IBS SSS</td>
<td>0.22 (-0.05, 0.51)</td>
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<tr>
<td>Group -&gt; IBS SSS</td>
<td>0.02 (-0.36, 0.41)</td>
</tr>
<tr>
<td>Group -&gt; Avoidance behaviour -&gt; IBS SSS</td>
<td>-0.11 (-0.29, -0.02)</td>
</tr>
<tr>
<td>R → safety behaviours → IBS-SSS</td>
<td>R → safety behaviours → WSA</td>
</tr>
<tr>
<td>Group -&gt; Safety behaviour</td>
<td>-0.96 (-1.24, -0.69)</td>
</tr>
<tr>
<td>Safety behaviour -&gt; IBS SSS</td>
<td>0.34 (0.13, 0.54)</td>
</tr>
<tr>
<td>Group -&gt; IBS SSS</td>
<td>0.23 (-0.14, 0.58)</td>
</tr>
<tr>
<td>Group -&gt; Safety behaviour -&gt; IBS SSS</td>
<td>-0.33 (-0.57, -0.11)</td>
</tr>
<tr>
<td>R → cognitions → anxiety → IBS-SSS</td>
<td>R → cognitions → anxiety → WSA</td>
</tr>
<tr>
<td>Group -&gt; Cognitions</td>
<td>-0.51 (-0.77, -0.25)</td>
</tr>
<tr>
<td>Cognitions → Anxiety</td>
<td>0.71 (0.57, 0.85)</td>
</tr>
<tr>
<td>Anxiety → IBS SSS</td>
<td>0.59 (0.41, 0.79)</td>
</tr>
<tr>
<td>Group → Cognitions → Anxiety → IBS-SSS</td>
<td>-0.21 (-0.38, -0.09)</td>
</tr>
<tr>
<td>R → safety behaviours → anxiety → IBS-SSS</td>
<td>R → safety behaviours → anxiety → WSA</td>
</tr>
<tr>
<td>Group → Safety behaviour → Anxiety</td>
<td>-0.96 (-1.24, -0.68)</td>
</tr>
<tr>
<td>Safety behaviour → Anxiety</td>
<td>0.34 (0.21, 0.46)</td>
</tr>
<tr>
<td>Anxiety → IBS SSS</td>
<td>0.34 (0.05, 0.61)</td>
</tr>
<tr>
<td>Group → Safety Behaviour → Anxiety → IBS SSS</td>
<td>-0.11 (-0.24, -0.01)</td>
</tr>
<tr>
<td>Symptom Severity</td>
<td>Work and social adjustment</td>
</tr>
<tr>
<td>------------------</td>
<td>---------------------------</td>
</tr>
<tr>
<td></td>
<td>b (95% CI)</td>
</tr>
<tr>
<td></td>
<td>WSA</td>
</tr>
</tbody>
</table>
Simple mediation models

The four variables of interest as mediators, GI related cognitions, avoidance behaviour, safety behaviour and anxiety were initially studied using simple mediation models.

Simple mediation models, each in turn including anxiety, GI related cognitions and GI safety behaviours, fitted the data well (table 2). Anxiety significantly mediated the effect of treatment on symptom severity ($b=-0.26, CI [-0.46 to -0.11], p=.004$) and WSA ($b=-0.35, CI [-0.56 to -0.16], p=.001$). GI related cognitions were a significant mediator of CBT treatment on symptom severity ($b=-0.24, CI [-0.43 to -0.09], p=.005$) and WSA (table 2). Safety behaviour was also a significant mediator for symptom severity ($b=-0.33, CI [-0.57 to -0.11], p=.005$) and WSA ($b=-0.35, CI [-0.60 to -0.14], p=.004$). Avoidance behaviour did not mediate the effect of treatment on either outcome (table 2). Figure 3 shows the standardized indirect effects with the 95% confidence intervals across the four mediators tested. The mediated effects were negative as we expected, because they are products of the negative effect of the treatment on the mediator and the positive effect of the mediator on the outcome. CBT compared to control gave a negative parameter estimate for the effect of the treatment on the mediator, i.e. the mediator values were lower (better) on average in the CBT group compared to the control group. The effect of the mediator on the outcome gave a positive effect estimate because for every standard deviation increase in the mediator (worsening), there was an increase (worsening) in the outcome. The significant indirect effects were similar sizes.
**Figure 3**: Standardized indirect effect sizes for each mediator variable in simple mediation models with 95% confidence intervals. A) Symptom severity outcome, B) Work and social adjustment outcome.

**Sequential Mediation Models**

*Full and partial mediation models*

Comparisons of sequences modelled as full or partial mediation models for the outcome of symptom severity showed that full mediation models fit the best for all mediation sequences (appendix E) apart from the sequence R → anxiety → GI safety behaviours → symptom severity (model 8a, table 2), where there was little difference in the fit of the models. Comparisons of full and partial mediation models on the WSA found that all sequences fit better as full mediation models (models 5b to 8b, table 2). While most of the differences seen in AIC and BIC between full and partial models were greater than two units, they were generally small (appendix E).
**Figure 4:** Standardised effect sizes of the indirect effects testing in sequential mediation models with 95% confidence intervals. Panel A: outcome of symptom severity. Panel B: outcome of work and social adjustment. 

**GI related cognitions and Anxiety**

In line with our hypothesis, the sequence $R \rightarrow GI \rightarrow C \rightarrow A \rightarrow SS$ (appendix D, panel A) showed the best fit to the data with a good fit according to the $\chi^2$ GOF and the CFI model fit criteria (table 2, model 5a). The lower AIC and BIC of 61 and 57 units respectively indicated that change in GI related cognitions preceding change in anxiety was more plausible than change in anxiety preceding change in GI related cognitions. The indirect effect was significant ($b= -0.22, CI [-0.40 to -0.90], p=.005$) and indicated that reduction in unhelpful GI related cognitions, resulted in a reduction of anxiety and this lead to the subsequent reduction in symptom severity (table 3). The same sequence was found to have the best fit for the outcome of WSA as well (appendix D, panel B), with lower AIC and BIC criteria (table 2, model 5b). The indirect effect here was also significant ($b= -0.26, CI [-0.44 to -0.11], p=.003$). For both outcomes, the path in which change in GI related cognitions preceded reductions in anxiety, had the largest standardised indirect effect compared across all sequential mediation models (figure 4).

**Behaviours and Anxiety**
As avoidance behaviour was not a significant mediator in the basic mediation models, this was not
taken forward into a sequential model, and only GI safety behaviours were studied. Concurrent with
our hypothesis, the sequence R \( \rightarrow \) GI safety behaviours \( \rightarrow \) anxiety \( \rightarrow \) symptom severity fit the data best
(appendix D, panel B). This had a good fit according to the CFI and \( \chi^2 \) GOF and an acceptable fit
according to the RMSEA and TLI (table 2, model 7a). However, the AIC and BIC provided relatively weak
support for the model where anxiety preceded GI safety behaviours, conflicting somewhat with the
results of the other fit indices (table 2, model 8a). On balance we proceeded with the GI safety
behaviours \( \rightarrow \) anxiety model, where the indirect effect was significant \((b=-0.11, CI [-.24 to -.01],
p=.049)\) with improvement (decrease) in GI safety behaviours and anxiety causing an improvement
(decrease) in symptom severity (table 3).

This sequence in which safety behaviour changed before anxiety reduction, was also shown to fit the
data best for WSA (appendix D, panel D). The CFI indicated good fit and the RMSEA indicated
acceptable fit, however the TLI, \( \chi^2 \) GOF did not indicate good model fit (table 2, model 7b). As for
symptom severity, the AIC and BIC provided more support for the reverse sequence (R \( \rightarrow \) anxiety \( \rightarrow \) GI
safety behaviours) mediation model. Having given priority to RMSEA and CFI values, we therefore took
forward the mediation model with superior RMSEA and CFI values (R \( \rightarrow \) GI safety behaviours \( \rightarrow \)
anxiety \( \rightarrow \) outcome). We found that the indirect effect was significant \((b=0.12, CI [-.23 to -.03],
p=.03)\) indicating that as mediating variables decreased, WSA also decreased (table 3).

**Discussion**

Our paper aimed to establish whether illness-related cognitions, avoidance and safety behaviours and
anxiety were significant mediators of treatment effect on the outcomes of symptom severity and WSA.
Change in GI related cognitions, GI related safety behaviours and general anxiety were found to
mediate the effect of CBT on both outcomes. However, avoidance behaviour was not a significant
mediator. The secondary aim of the paper was to elucidate whether GI related cognitive and
behavioural change preceded changes in anxiety or vice versa. The results were supporting of
endogenous models of IBS, indicating that cognitive and behavioural (safety behaviours) responses
specific to IBS changed prior to a reduction in general anxiety. This sequence was found to best explain
the treatment effect on both outcomes. These results suggest that targeting change in such processes are necessary to reduce both anxiety and consequently symptom severity and impaired WSA.

**Mechanisms of Treatment**

The results of our basic mediation analyses provided some support for both endogenous and exogenous models of IBS. The finding that GI related cognitions and GI safety behaviours significantly mediated the treatment effect on both outcomes lends support to endogenous models of IBS. This fits with findings from previous mediation studies conducted in CBT trials for IBS, which have demonstrated the mechanistic roles of cognitions, behaviours and GI specific anxiety [16]. However, the finding that general anxiety was also a significant mediator provides some support for exogenous models of IBS. These models identify stress (or anxiety) external to IBS as a key maintaining factor of IBS symptoms and therefore important to change in psychological treatment. Furthermore, it was surprising to find that avoidance behaviour was not a significant mediator. The paths from avoidance behaviour to outcome in the simple mediation models for both outcomes were not significant, suggesting that change in avoidance behaviour was not related to outcome. In contrast, significant paths from randomisation to avoidance behaviour at 1.5 months follow up indicated that CBT, at least initially, reduced avoidance behaviours (table 3). Such findings suggest that change in avoidance does not result in reductions in symptom severity or enhanced functioning.

A recent study assessing the mediating properties of avoidance behaviour, GI specific anxiety, self-efficacy and non-reactivity in CBT-IE compared to CBT without exposure (CBTWE) [25] could explain this finding. This study found that both avoidance behaviour and GI specific anxiety mediated the additional benefit of CBT-IE compared to CBTWE. It could be that in a treatment protocol that utilises more exposure-based techniques to target GI specific anxiety and hypervigilance, avoidance behaviour has more of a mechanistic role. Furthermore, moderated mediation analysis indicated that the mediated effect of avoidance was larger for participants who had high avoidance at baseline. This too offers an explanation for our results: in the absence of assessing moderated mediation, our analysis may not have detected avoidance behaviour as a mediator for a portion of the sample. Alternatively,
our overall sample may not have had sufficiently high baseline avoidance for this to be a significant mediator. Other reasons for this finding are considered further under limitations.

Our results demonstrate the importance of GI safety behaviours in the maintenance of symptoms and disruption to work and social functioning in IBS. Safety behaviours, such as excessive straining on the toilet or the use of medications to prevent symptoms, have been shown to disrupt bowel functioning and motility [56, 57]. Furthermore, individuals with IBS have reported that engaging in behaviours such as taking preventative medication and wearing protective underwear has a substantial impact on their daily lives [58, 59]. These results highlight that changing such behaviours is an important component of therapy. While some CBT protocols target a reduction of endogenous stress and focus on changing these symptom-specific behaviours, other protocols focus primarily on reducing exogenous stress and may not target safety behaviours.

The sequential models in both the previous mediation study using this data and the present study demonstrate that a three system’s CBT treatment is effective in changing GI related cognitions and safety behaviours. The previous results indicated that behaviour change preceded cognitive change [22], suggesting behaviour change may facilitate the modification of cognitions. The present results demonstrate that GI specific cognitive and behavioural change precedes reduction in general anxiety. This fits with previous research in anxiety disorders and health anxiety, which has suggested that targeting the use of safety behaviours is necessary for the reduction of anxiety [35, 60, 61] and improving illness trajectories [62].

Together, these results provide further support for endogenous models of IBS. As IBS specific responses are shown to be of primary importance for changing outcomes we may consequently infer that these are key maintaining processes in IBS. In contrast, if IBS was primarily maintained by stress/anxiety external to IBS (e.g. general anxiety, life events) we may expect treatment to operate primarily by reducing general anxiety. To better assess the mechanistic value of external (or general) stress/anxiety versus IBS-specific stress (or GI related cognitive, behavioural and affective responses), a parallel mediator model could be used to quantify the mediating effects of each type of mediator.

Limitations
The present study did not collect a measure of GI specific anxiety, such as that measured by the visceral sensitivity index [63]. Consequently, we were not able to compare the mediating effect of general versus IBS-specific anxiety. The dichotomy between endogenous and exogenous stress in IBS may also be inadequate, as stress can be internal and external to IBS within the same individual.

It is recommended that mediators are measured at least once during treatment [14]. However, assessments in the original trial were only taken post treatment (aside from pre-treatment measures). Therefore, the mediational change occurred after treatment had finished. The mediational processes following treatment may differ to those that occur during treatment. Furthermore, there is a large time difference between the mediator measured at 1.5 and 3 months and the outcome at 12 months. Future studies should aim to include measurements at closer intervals for the purpose of assessing mediation [14] as has been conducted in previous mediation studies in IBS [17, 25].

Our analysis was conducted in the context of a waning treatment effect at the 12 month follow up in order to preserve temporal sequencing of variables [12]. Future mediational studies with similar follow up periods are needed to ascertain whether the results are replicated when the treatment effect is still observed. Nevertheless, assessing mediation in the context of no treatment effect is now widely considered valid and important [45, 46, 64]. It allows us to gather information about where in the theoretical mediation pathway treatment fails. This can help us to refine and improve treatments. The treatment in the present study had a significant effect up until the 3 month follow up. The decline in treatment effect may be attributable to the lack of mechanistic effect found in avoidance behaviour. This has previously been found to significantly mediate the treatment effect of CBT-IE in IBS [25]. Although in the present study avoidance behaviour was changed by treatment, it may be that the reduction in such behaviour was not sufficient to sustain the efficacy of the treatment effect at 12 months. It may be that the inclusion of more interoceptive exposure techniques as used in CBT-IE may be beneficial to the long-term effects of treatment by increasing the magnitude of treatment effect on avoidance behaviour reduction.
The final models with best fit were the full mediation models, which may in part be due to the lack of a sustained treatment effect i.e. there were no direct effects of treatment on outcome, yet there were significant indirect effects. It is, however, unlikely that our models included all possible mediators (such as GI specific anxiety). Future analysis would ideally include all hypothesised mediators in a model. Our study was also limited by a relatively small sample size, which may increase the probability of type II error [43].

Finally, IBS is a heterogeneous population with varying degrees of symptom severity, impairment and psychosocial impact [65, 66]. The two moderated mediation studies conducted to date have indicated that mechanisms of change may differ based on different patient characteristics at baseline [25, 67]. Our analysis was not designed to assess this and therefore may provide an incomplete picture of treatment mechanisms across the IBS population.

**Strengths**

The present study used robust methodology to study the mediation effects of CBT in IBS. Unlike other studies reviewed [16], the inclusion of mediator variables were theoretically informed and assessed at adequate intervals to allow temporal precedence, increasing the plausibility of interpreting effects as causal. Effects of mediator and outcome variables measured at baseline on the mediated effect and outcome were controlled for, to reduce the potential for residual confounding of the non-randomised mediator-outcome relationships in the models. In addition, the mediation analysis was conducted using data from an RCT, which further reduces the potential for confounding factors where the treatment is randomised.

**Conclusion**

Our results suggest that CBT treatments for IBS should target change in IBS specific cognitive and behavioural responses to symptoms as these processes lead to reduction in general anxiety and subsequent improvement in symptom severity and adjustment. These findings are in line with endogenous stress models of IBS. However, the results also indicate a mechanistic role of general
anxiety. Future studies should seek to assess whether this effect remains significant when GI specific anxiety is included in the mediation models.

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**Declaration of Interest**

None

**Competing Interests**

The authors have no competing interests to report

**Ethical Standards**

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008

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Appendix A

Supplementary Material

Physical sensations (experience of symptoms)
Anxiety

Gastrointestinal related behaviours
- Straining on toilet
- Checking stools
- Avoiding foods
- Carrying medication

Gastrointestinal related cognitions
- “Symptoms are too much to handle”
- “Can’t concentrate due to pain”

Figure of Three Systems Model in IBS

Appendix B

Methodology regarding selection of partial versus full mediation models

Partial versus full mediation
In mediation the total effect of an independent variable (e.g. treatment) on an outcome can be partitioned into the direct effect (path R to O, figure 1) and the indirect effect (paths from R to O via M, figure 1). The indirect effect quantifies the extent to which the treatment effect on the outcome is transmitted via the mediator (mediated effect). The direct effect quantifies the remaining direct effect of treatment on the outcome. We use the term full mediation model to describe a model explicitly assuming the direct effect is essentially equal to zero, allowing for no direct pathway between treatment and outcome, and so postulate that the full effect of the outcome is transmitted via the mediating variable (full mediation model, figure 1). Models we describe as partial mediation models allow for both direct and indirect pathways (models 1-4 and the partial mediation model, figure 1). In this latter type of model, we can assess whether mediation is partial or full; if there is full mediation, the mediated effect will be statistically significant, with a non-significant direct effect. If the mediated and direct effects are statistically significant, this indicates partial mediation.
The first four models assessed mediation via a single mediator (figure 1). In figure 1, full and partial sequential mediation models are illustrated. Each sequence (e.g. R → GI related cognitions → anxiety → outcome) was tested in the context of a partial mediation model and a full mediation model, and the best fitting model was assessed using the AIC and BIC criteria. This followed the process of the previous mediation paper (Reme, Stahl et al, 2011; Kennedy, Jones et al. 2005) and was used to determine whether the inclusion of a direct path from randomisation to outcome enhanced or detracted from the fit of the models to the data. Once a full or partial mediation model was selected, each sequence was compared using the model fit indices described above. The mediated effect of all models assessed calculated confidence intervals using bootstrap resampling with 1000 repetitions and 95% confidence interval (Chalder, Goldsmith, White, Sharpe, & Pickles, 2015; Efron & Tibshirani, 1994; Shrout & Bolger, 2002; Williams & MacKinnon, 2008).


Appendix C

A

B

Trajectory of primary outcomes
Appendix D

Best fitting models as indicated by standardised indirect effect size for symptom severity and work and social adjustment (WSA). Single headed arrows indicate hypothesized relationships between variables with standardized regression coefficients next to each path with 95% confidence intervals in brackets. Not shown in the diagrams for simplicity are the paths indicating the baseline outcome and mediator variables controlled for by including these as predictors for each dependent variable included in the model.
Appendix E

Comparison of model fit indices for full versus partial mediation models of sequences

<table>
<thead>
<tr>
<th>Symptom Severity</th>
<th>Full/Partial Model</th>
<th>RMSEA [90% CI]</th>
<th>CFI</th>
<th>TLI</th>
<th>AIC</th>
<th>BIC</th>
<th>( \chi^2 ) GOF</th>
<th>Indirect effect</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>R \rightarrow C \rightarrow A \rightarrow IBS-SS</td>
<td>Full</td>
<td>0.070 [0, 0.14]</td>
<td>0.981</td>
<td>0.952</td>
<td>2111.6</td>
<td>2198.5</td>
<td>( \chi^2(6)=10.38, p=.11 )</td>
<td>.006</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Partial</td>
<td>0.083 [0, 0.16]</td>
<td>0.977</td>
<td>0.932</td>
<td>2113.3</td>
<td>2203.2</td>
<td>( \chi^2(5)=10.15, p=.07 )</td>
<td>.006</td>
<td></td>
</tr>
<tr>
<td>R \rightarrow A \rightarrow C \rightarrow IBS-SS</td>
<td>Full</td>
<td>0.102 [0, 0.17]</td>
<td>0.949</td>
<td>0.872</td>
<td>2174.0</td>
<td>2260.9</td>
<td>( \chi^2(6)=15.20, p=.02 )</td>
<td>.01</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Partial</td>
<td>0.117 [0.05, 0.19]</td>
<td>0.944</td>
<td>0.831</td>
<td>2176.0</td>
<td>2266.0</td>
<td>( \chi^2(5)=15.16, p=.01 )</td>
<td>.01</td>
<td></td>
</tr>
<tr>
<td>R \rightarrow SB \rightarrow A \rightarrow IBS-SS</td>
<td>Full</td>
<td>0.08 [0, 0.15]</td>
<td>0.976</td>
<td>0.939</td>
<td>2218.9</td>
<td>2305.8</td>
<td>( \chi^2(6)=11.17, p=.08 )</td>
<td>.006</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Partial</td>
<td>0.09 [0, 0.16]</td>
<td>0.975</td>
<td>0.924</td>
<td>2220.1</td>
<td>2310.0</td>
<td>( \chi^2(5)=10.42, p=.06 )</td>
<td>.006</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Work and Social Adjustment</th>
<th>Full/Partial Model</th>
<th>RMSEA [90% CI]</th>
<th>CFI</th>
<th>TLI</th>
<th>AIC</th>
<th>BIC</th>
<th>( \chi^2 ) GOF</th>
<th>Indirect effect</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>R \rightarrow C \rightarrow A \rightarrow WSA</td>
<td>Full</td>
<td>0.151 [0.10, 0.21]</td>
<td>0.929</td>
<td>0.822</td>
<td>1974.8</td>
<td>2061.8</td>
<td>( \chi^2(6)=26.20, p&lt;.001 )</td>
<td>.002</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Partial</td>
<td>0.166 [0.11, 0.23]</td>
<td>0.928</td>
<td>0.785</td>
<td>1976.0</td>
<td>2065.9</td>
<td>( \chi^2(5)=25.33, p&lt;.001 )</td>
<td>.002</td>
<td></td>
</tr>
<tr>
<td>R \rightarrow A \rightarrow C \rightarrow WSA</td>
<td>Full</td>
<td>0.160 [0.10, 0.22]</td>
<td>0.911</td>
<td>0.777</td>
<td>2018.6</td>
<td>2105.5</td>
<td>( \chi^2(6)=28.63, p&lt;.001 )</td>
<td>.003</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Partial</td>
<td>0.177 [0.12, 0.24]</td>
<td>0.908</td>
<td>0.724</td>
<td>2020.2</td>
<td>2110.2</td>
<td>( \chi^2(5)=28.29, p&lt;.001 )</td>
<td>.003</td>
<td></td>
</tr>
<tr>
<td>R \rightarrow SB \rightarrow A \rightarrow WSA</td>
<td>Full</td>
<td>0.096 [0.03, 0.16]</td>
<td>0.966</td>
<td>0.914</td>
<td>2146.3</td>
<td>2233.2</td>
<td>( \chi^2(6)=14.18, p=.03 )</td>
<td>.03</td>
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</tr>
<tr>
<td></td>
<td>Partial</td>
<td>0.105 [0.04, 0.18]</td>
<td>0.966</td>
<td>0.898</td>
<td>2147.2</td>
<td>2237.2</td>
<td>( \chi^2(5)=13.10, p=.02 )</td>
<td>.03</td>
<td></td>
</tr>
<tr>
<td>R \rightarrow A \rightarrow SB \rightarrow WSA</td>
<td>Full</td>
<td>0.115 [0.06, 0.18]</td>
<td>0.954</td>
<td>0.884</td>
<td>2125.8</td>
<td>2212.7</td>
<td>( \chi^2(6)=17.66, p=.007 )</td>
<td>.02</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Partial</td>
<td>0.131 [0.07, 0.20]</td>
<td>0.950</td>
<td>0.849</td>
<td>2127.8</td>
<td>2217.7</td>
<td>( \chi^2(6)=17.66, p=.003 )</td>
<td>.02</td>
<td></td>
</tr>
</tbody>
</table>

Rows in bold indicate best fitting model; RMSEA, root mean square error of approximation; CFI, comparative fit index; TLI, Tucker-Lewis Index; AIC, Akaike’s Information Criterion; BCC, Brown-Cudeck criteria; \( \chi^2 \) GOF, Chi square goodness of fit. R. randomisation; A, general anxiety; C, GI related cognitions; SB, GI safety behaviours; WSA, work and social adjustment; SS, symptom severity.
Highlights

- Change in gastrointestinal cognitions, gastrointestinal safety behaviours and general anxiety mediate treatment effect of cognitive behavioural therapy on the outcomes of symptom severity and work and social adjustment in IBS
- Change in gastrointestinal cognitions precede reduction in general anxiety
- Change in gastrointestinal safety behaviours precede reduction in general anxiety
- Change in gastrointestinal avoidance behaviour was not a mediator of treatment effect
- Psychological treatments in IBS should target gastrointestinal specific responses for change in IBS