# INPLASY PROTOCOL

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**Review Stage at time of this submission:** **The review has not yet started.**

**Conflicts of interest:**
**None declared.**

# Abnormalities of intrinsic brain activity in irritable bowel syndrome (IBS): a protocol for systematic review and meta-analysis of resting-state functional imaging

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**Review question / Objective:** **Studies of abnormal regional homogeneity (ReHo) in irritable bowel syndrome (IBS) have reported inconsistent results. Therefore, we conducted a meta-analysis using the Seed-based d Mapping software package to identify the most consistent and replicable findings.**
**Eligibility criteria:** **Studies that satisfied the following conditions were included in the meta-analysis: (i) patients had been diagnosed with idiopathic IBS; (ii) ReHo comparison of patients with idiopathic IBS versus healthy controls was conducted; (iii) three-dimensional coordinates (Talairach or Montreal Neurological Institute [MNI]) were reported for the whole-brain ReHo analysis; (iv) significant results were reported using thresholds for significance corrected for multiple comparisons or uncorrected with spatial extent thresholds; and (v) the study was published as an original article (not as a letter or an abstract) in a peer-reviewed English language journal. Datasets were excluded if they explicitly indicated patients with IBS diagnosed with comorbid neurological or psychiatric diseases.**

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 March 2021 and was last updated on 30 March 2021 (registration number INPLASY202130108).

## INTRODUCTION

**Review question / Objective:** **Studies of abnormal regional homogeneity (ReHo) in irritable bowel syndrome (IBS) have reported inconsistent results. Therefore, we conducted a meta-analysis using the Seed-based d Mapping software package to identify the most consistent and replicable findings.**

**Condition being studied:** Irritable bowel syndrome (IBS) is one of the most common functional gastrointestinal (GI) disorders affecting up to 11.5% of the general global population. According to Rome III criteria, IBS was divided into three clinical subtypes: IBS with diarrhea (IBS-D), IBS with constipation (IBS-C), and IBS with a mixed bowel pattern (IBS-M). IBS-D is the most common subtype of IBS and has a lower disease-specific quality of life than do the other two subtypes. Current treatment options for IBS-D are limited. Resting-state fMRI is a more important tool to examine brain functional activities of IBS when intestinal tract is at rest state. Based on the amplitude of low-frequency fluctuation (ALFF) and rsfMRI, Ma et al. applied rsfMRI and the amplitude of low-frequency fluctuation (ALFF) method in IBS patients and found that the left superior frontal gyrus, right MFG, right hippocampus, right superior temporal pole, and bilateral postcentral gyrus exhibited lower ALFF values, while the left calcarine and left median cingulate exhibited higher ALFF values. There was a significant correlation between duration of disease in IBS and ALFF values in the altered regions . Qi et al. reported that IBS patients had decreased ALFF values in several core default mode network regions and increased ALFF values in the bilateral posterior insula and cuneus. However, the brain function of IBS-D patients during resting-state is still unclear. Therefore, we chose IBS-D patients as research subjects. All subjects underwent rsfMRI. fALFF was calculated to analyze the rsfMRI data. Considering the role of psychosocial factors in IBS, we hypothesized that IBS-D patients have abnormal activity in emotional and cognitive areas.

## METHODS

**Participant or population:** Adult with clinic and laboratory evidence to support the clinical diagnosis of IBS.

**Intervention:** NA.

**Comparator:** Normal people.

**Study designs to be included:** Published randomized controlled trials.

**Eligibility criteria:** Studies that satisfied the following conditions were included in the meta-analysis: (i) patients had been diagnosed with idiopathic IBS; (ii) ReHo comparison of patients with idiopathic IBS versus healthy controls was conducted; (iii) three-dimensional coordinates (Talairach or Montreal Neurological Institute [MNI]) were reported for the whole-brain ReHo analysis; (iv) significant results were reported using thresholds for significance corrected for multiple comparisons or uncorrected with spatial extent thresholds; and (v) the study was published as an original article (not as a letter or an abstract) in a peer-reviewed English language journal. Datasets were excluded if they explicitly indicated patients with IBS diagnosed with comorbid neurological or psychiatric diseases.

**Information sources:** A comprehensive search of studies conducted in the PubMed, Embase, and Web of Science databases.

**Main outcome(s):** ReHo differences between patients with IBS and healthy controls was conducted using the SDM software package (version 4.31 for Windows) in a standard process (www.sdmproject.com).

**Quality assessment / Risk of bias analysis:** A heterogeneity analysis was conducted used a random effects model with Q statistics to explore unexplained between-study variability in the results. Heterogeneous brain regions were obtained using the default SDM kernel size and thresholds (FWHM = 20 mm, p = 0.005, uncorrected for FDR, peak height Z = 1, cluster extent = 10 voxels) . In addition, Egger's test was performed using the Stata/SE 12.0 software for Windows to assess possible publication bias by extracting the values from statistically significant relevant peaks between patients with PD and healthy controls . A p-value less than 0.05 was considered significant.

**Strategy of data synthesis:** Voxel-wise meta-analysis: A meta-analysis of ReHo differences between patients with PD and healthy controls was conducted using the SDM software package (version 4.31 for Windows) in a standard process (www.sdmproject.com). The SDM approach has been thoroughly described elsewhere. In brief, we first extracted peak coordinates and effect sizes (e.g., t-values) of differences in ReHo between patients with PD and healthy controls from each dataset. A standard MNI map of the ReHo differences was then separately recreated for each dataset using an anisotropic Gaussian kernel. The mean map was finally generated by voxel-wise calculation of the random-effects mean of the dataset maps, weighted by the sample size, intra-dataset variability, and between-dataset heterogeneity. To optimally balance false positives and negatives, we used the default SDM kernel size and thresholds (full width at half maximum [FWHM] = 20 mm, p = 0.005, uncorrected for FDR, peak height Z = 1, cluster extent = 10 voxels). It should be noted that this FWHM kernel is intended to assign indicators of proximity to reported coordinates but not to smooth any image that is different in nature. If necessary, a subgroup meta-analysis was further conducted.

**Subgroup analysis:** NA.

**Sensitivity analysis:** Jackknife sensitivity analysis: Following preprocessing of the data, a whole-brain voxel-based jackknife sensitivity analysis was performed to test the robustness of the findings by iteratively repeating the same analysis, excluding one dataset each time.

**Country(ies) involved:** China.

**Keywords:** Irritable bowel syndrome; fMRI; ReHo.

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