Brain-Gut-Microbiome Differences between Women with Subtypes of Irritable Bowel Syndrome

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Background

- Irritable Bowel Syndrome (IBS) is a common female-predominant disorder of gut-brain interaction
- The constipation-predominant subtype of IBS (IBS-C) is almost twice as prevalent in women (40%) compared to men (21%) with IBS[1]
- The Brain-Gut-Microbiome (BGM) has been implicated in the pathophysiology of IBS
- Some studies suggest that individuals with IBS subtypes may have distinct alterations in brain connectivity,[2] while others have revealed different gut microbiomes,[3] but no study to date has used a systems biology approach to elucidate BGM alterations in IBS subtypes
- In an effort to explore the underlying mechanisms and physiology of IBS subtypes, we use a systems biology approach

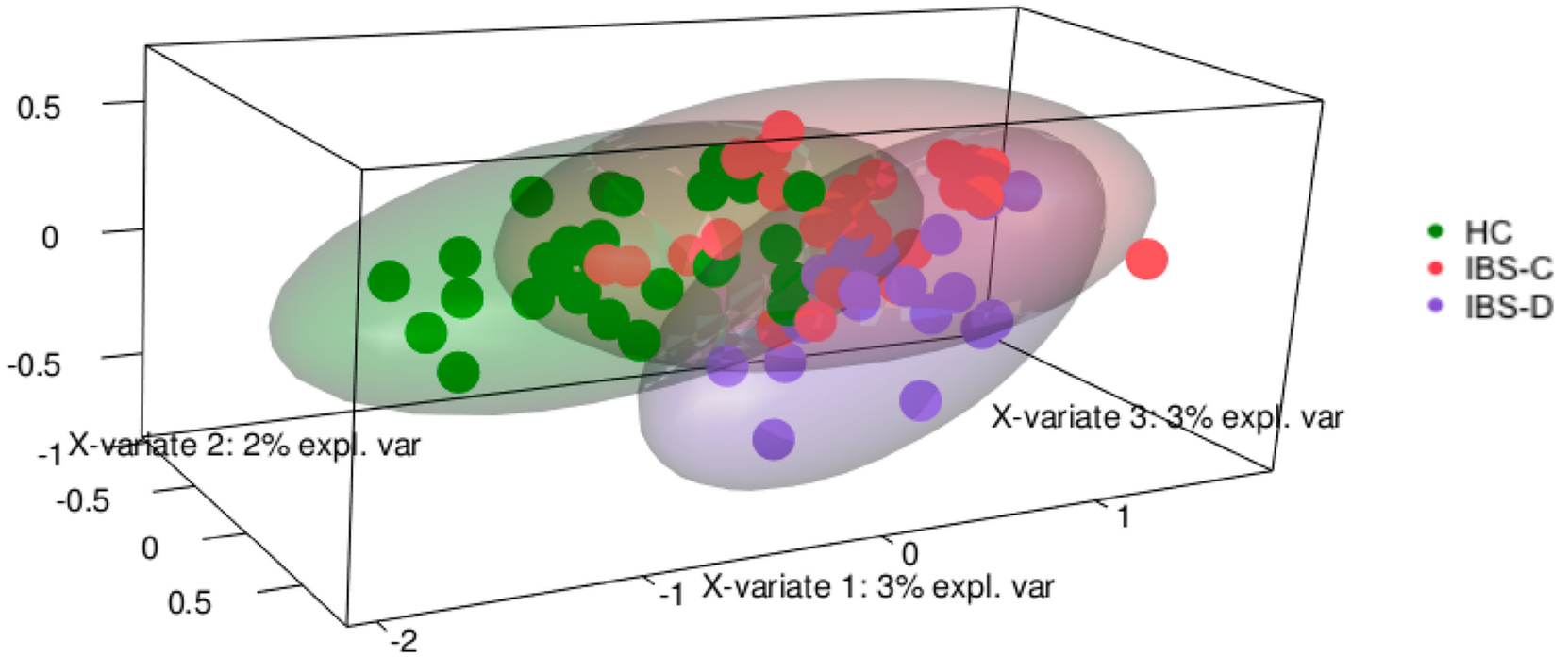
1. Kim et al., 2018. **2.** Weiqun et al., 2021 **3.** Hadjivasilis et al., 2019. **3.** Atkinson et al., 2006

Methods

- Cross-sectional study
- Fecal samples and resting state fMRI imaging were obtained from 138 premenopausal women
  - 36 IBS-C (constipation-predominant), 28 IBS-D (diarrhea-predominant), 35 IBS-M (mixed, alternating, and unspecific bowel habits), and 39 HCs (healthy controls). Differences were explored between IBS-C, IBS-D, and HC. IBS-M were excluded in our analyses
- Partial Least Squares Discriminant Analysis (PLS-DA) explored group differences
- Brain regions and fecal metabolites with PLS-DA VIP>1.0 assessed by Student's t-test
- Partial correlation analysis between significantly changed metabolites and neuroimaging data
- Controlled for age, BMI, and diet, FDR correction with $q<.05$ as significant (to correct for multiple comparisons)

Results

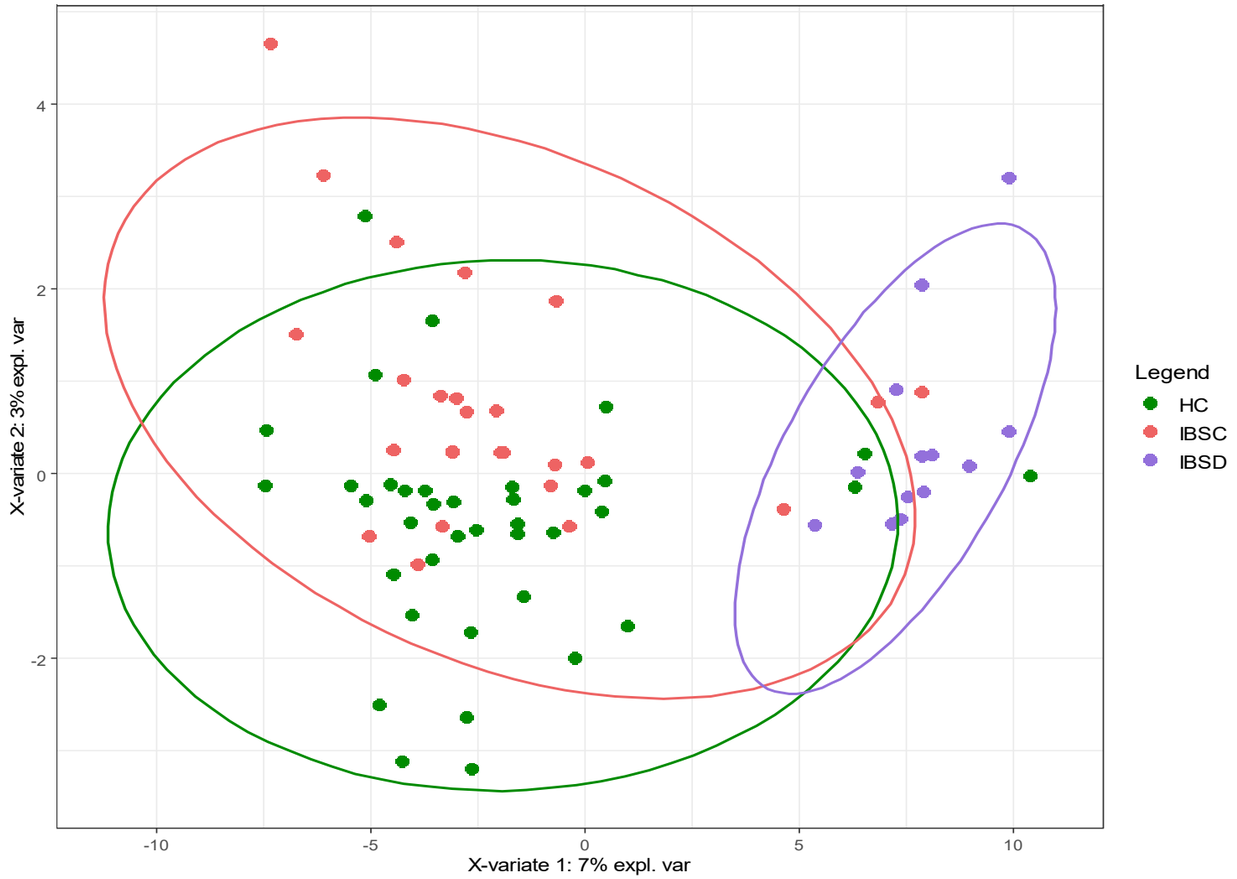
Figure 1. sPLS-DA Analysis of Brain Connectivity among IBS-C, IBS-D, and HC



- IBS-C, IBS-D, and HCs can be distinguished from each other by their alterations in functional links on MRI (“brain connectivity”) with an accuracy of 75%
- IBS-C had greater functional connectivity within the sensorimotor, default mode, and emotional regulation networks compared to IBS-D and HCs
- IBS-D had greater functional connectivity within the central executive network and the occipital cortex compared to IBS-C and HCs

Results, continued

Figure 2. sPLS-DA Analysis of Fecal Metabolites between IBS-C, IBS-D, and HC



Fecal metabolites differentiate IBS-C, IBS-D and HCs with an accuracy of 78%

In a separate, integrated analysis, IBS-D showed tryptophan-related metabolites that positively correlated with activity in sensory network regions on MRI (N-acetyltryptophan: r=0.38, p=0.04).

Conclusions

- This study is the first to integrate neuroimaging and microbiome data to characterize subtypes of IBS.
- IBS-C showed greater alterations in regions involved in the processing and perception of sensory signals and emotional arousal, while IBS-D showed greater alterations in those involved in decision-making and problem-solving.
- These brain patterns may enhance centrally-mediated visceral perception in IBS-C and IBS-D.
- Distinct fecal metabolite patterns in IBS subtypes, including the relationship between tryptophan-related metabolites and sensorimotor connectivity, may highlight the role of serotonin in the pathophysiology of IBS subtypes in premenopausal women.

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