KU LEUVEN

Neuroinflammation in irritable bowel syndrome: a [18F]DPA-714 PET study

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DISCOVERIE

LaBGAS
LABORATORY FOR BRAIN-GUT AXIS STUDIES

TARGID
TRANSLATIONAL RESEARCH IN GASTROINTESTINAL DISORDERS

Introduction

- Irritable bowel syndrome (IBS)
  - Disorder of gut-brain interaction
  - Abdominal pain and altered bowel habits

- High level of comorbidity with
  - mood and anxiety disorders
  - functional somatic disorders

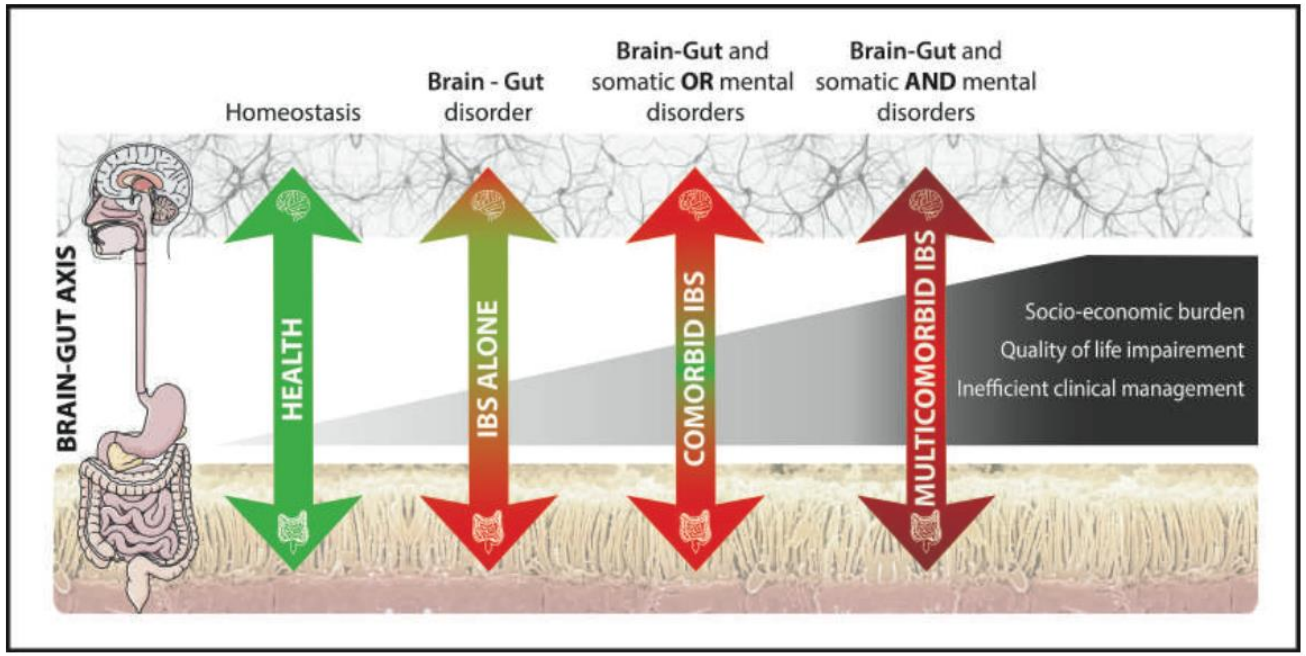

Figure credit: *Discoverie* consortium

Introduction

- Evidence for (low-grade) peripheral **immune dysregulation** in IBS

- Inflammation in the *CNS*, known as **neuroinflammation**, has been implicated in **mood and pain** disorders often comorbid with IBS

Neuroinflammation and depression: A review

Romain Troubat[1] | Pascal Barone[1] | Samuel Leman[1] | Thomas Desmidt[1,2] | Arnaud Cressant[1] | Boriana Atanasova[1] | Bruno Brizard[1] | Wissam El Hage[1,2] Alexandre Surget[1] | Catherine Belzung[1] | Vincent Camus[1,2]

Evidence of neuroinflammation in fibromyalgia syndrome: a [^{18}F]DPA-714 positron emission tomography study

Mueller, Christina[a,*]; Fang, Yu-Hua D.[b]; Jones, Chloe[c]; McConathy, Jonathan E.[d]; Raman, Fabio[d]; Lapi, Suzanne E.[d]; Younger, Jarred W.[c]

Author Information

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Review

Chronic pain and neuroinflammation

Pascale Vergne-Salle*, Philippe Bertin

Introduction

Neuroinflammation could contribute to

- Visceral hypersensitivity
- Comorbid mood and pain disorders
- High levels of fatigue
- Cognitive dysfunction
- Increased stress sensitivity

often seen in IBS

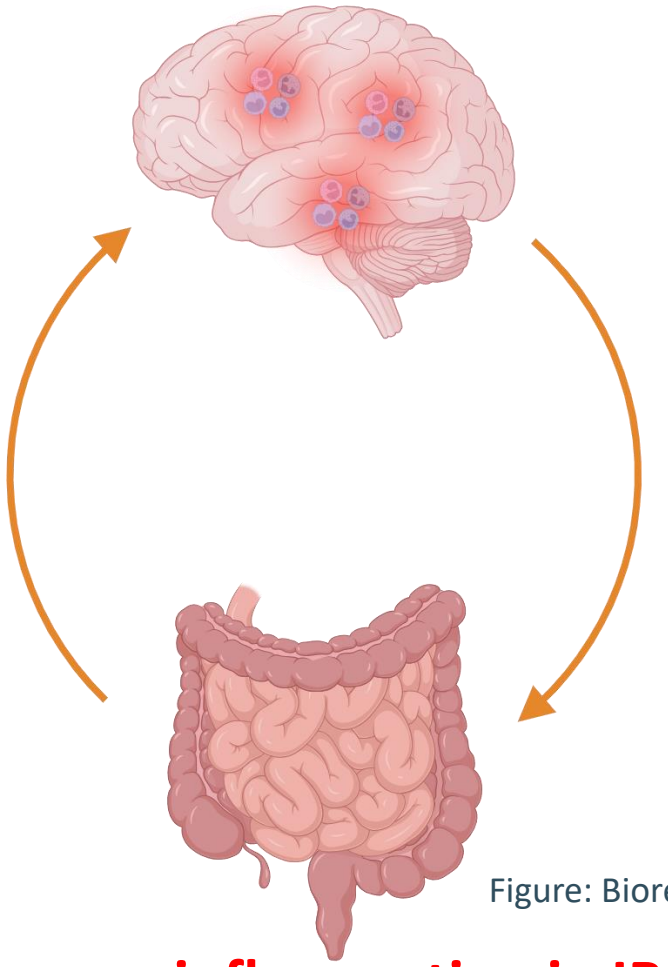


Figure: Biorender.com

However, currently **no studies directly investigating neuroinflammation in IBS**

Ishioh, Nozu, & Okumura, 2024, *Digestion;* Troubat et al., 2021, *European Journal of Neuroscience;* Vergne-Salle & Bertin, 2021, *Joint Bone Spine;* VanElzakker et al., 2019, *Frontiers in Neurology;* Daulatzai, 2014, *Neurochemical Research*

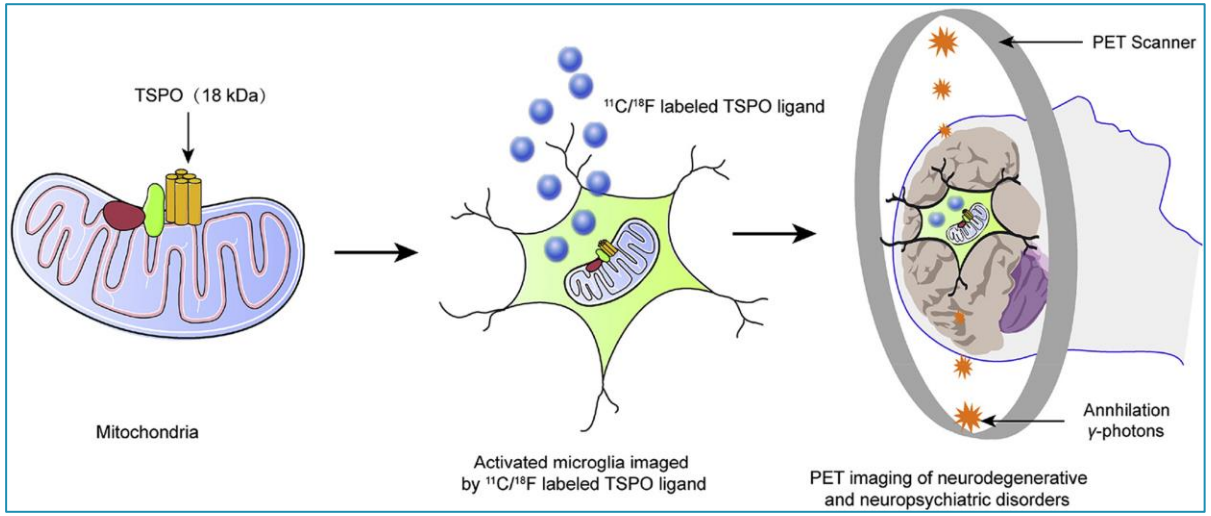
Measuring neuroinflammation

- Neuroinflammation: activation and increased density of **microglia and astrocytes** in the brain

- **Translocator protein (TSPO)** is upregulated with **increased microglial density**

- **PET imaging** with radiotracer that binds to TSPO in the brain (eg. [18F]DPA-714)

- **Total volume of distribution** (Vt) of radiotracer as a marker of neuroinflammation



From: Zhang et al., 2021, *Acta Pharmaceutica Sinica B*

Research questions

1) Do **IBS patients have increased levels of neuroinflammation** compared to healthy controls?

2) Within the IBS patient sample, is neuroinflammation **related to psychiatric and functional somatic comorbidity**?
   a. Comorbid vs. non-comorbid
   b. Correlation with comorbidity severity

Design

Screening

- IBS: Rome IV
- Psychiatric comorbidity: MINI interview
- Fibromyalgia and chronic fatigue syndrome criteria
- Comorbidity severity:
  - PHQ-9
  - GAD-7
  - MFI
  - FIQ

  ➔ Composite score

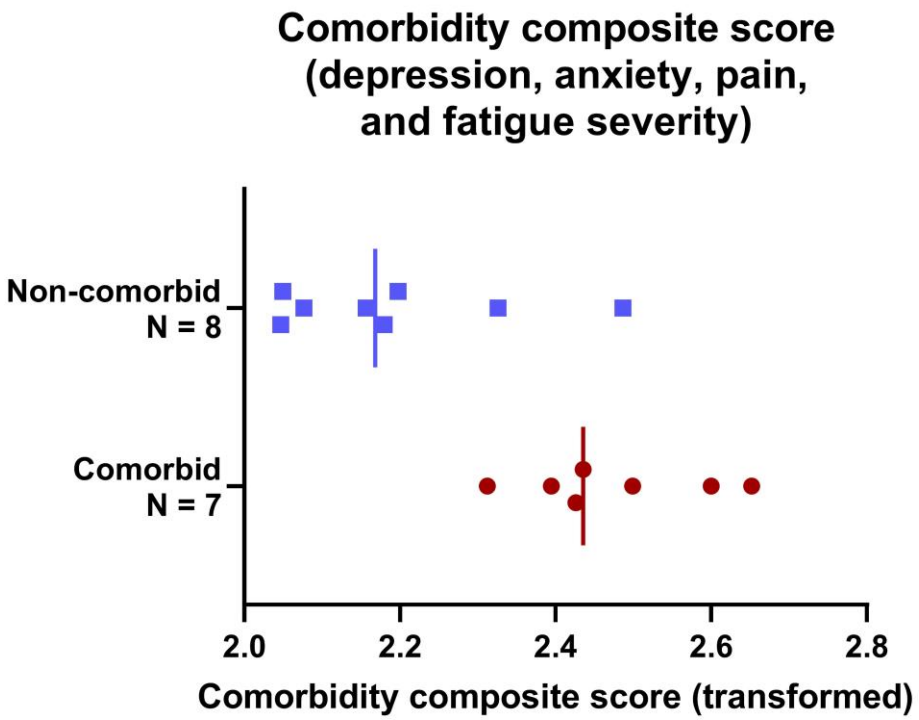
Figure: Biorender.com

Arterial sampling provides a time-activity curve allowing for kinetic modeling

Sample description: patients vs. HC

	IBS patients	Healthy controls
Sample size	15	15
Mean age (SD)	43.3 (13.4)	41.8 (13.6)
% women	53%	73%
Mean BMI (SD)	23.3 (4.3)	23.0 (3.2)

Sample description: IBS patients

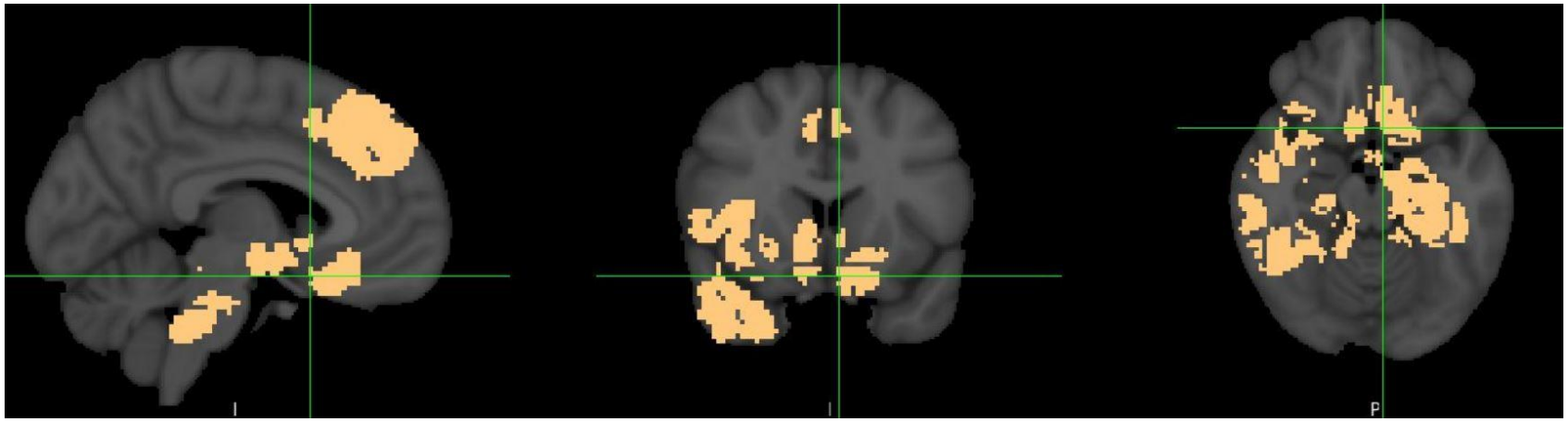


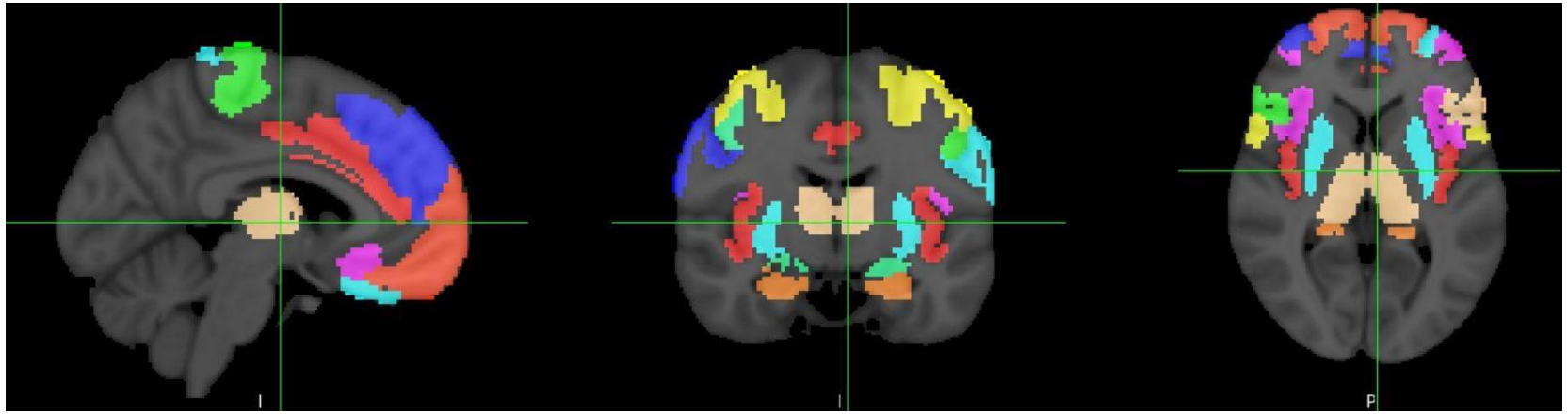
Comorbid: fulfilling diagnostic criteria of at least one of these:

- Depressive episode (past 2 years)
- Anxiety disorder
- Fibromyalgia
- Chronic fatigue syndrome

2 complimentary analysis methods

1. voxel-wise analysis using a mask containing brain regions associated with peripheral inflammation (Kraynak et al., 2018)

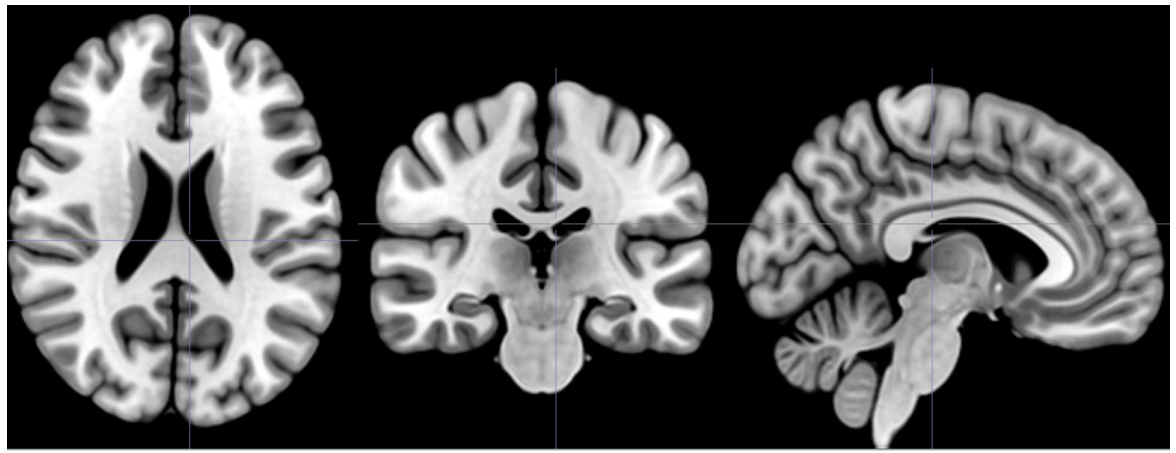




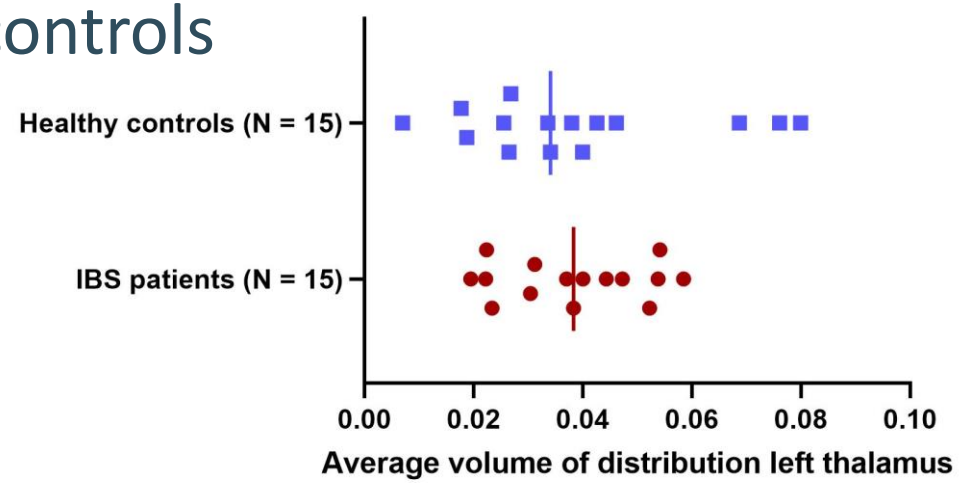
2. Region of interest analysis: averaging Vt within 17 bilateral regions of interest. ROIs with evidence for case-control differences in TSPO expression in psychiatric or pain disorders (De Picker et al., 2023)

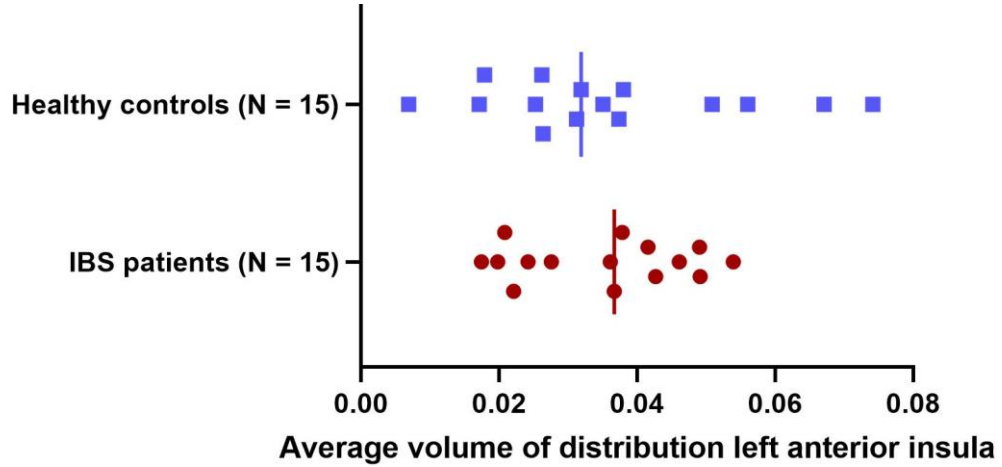
Results

1. Neuroinflammation in patients vs. healthy controls



Voxel-wise analysis: no significant differences

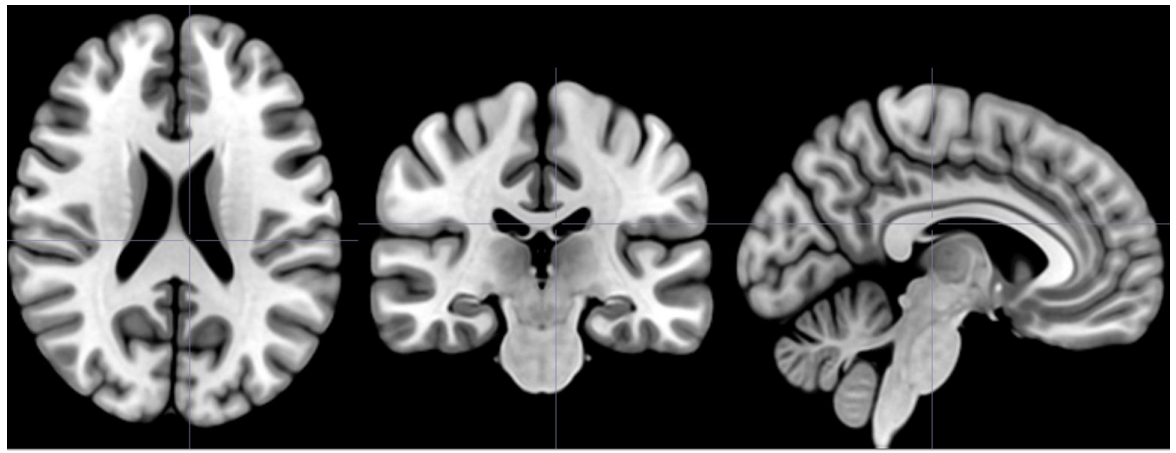




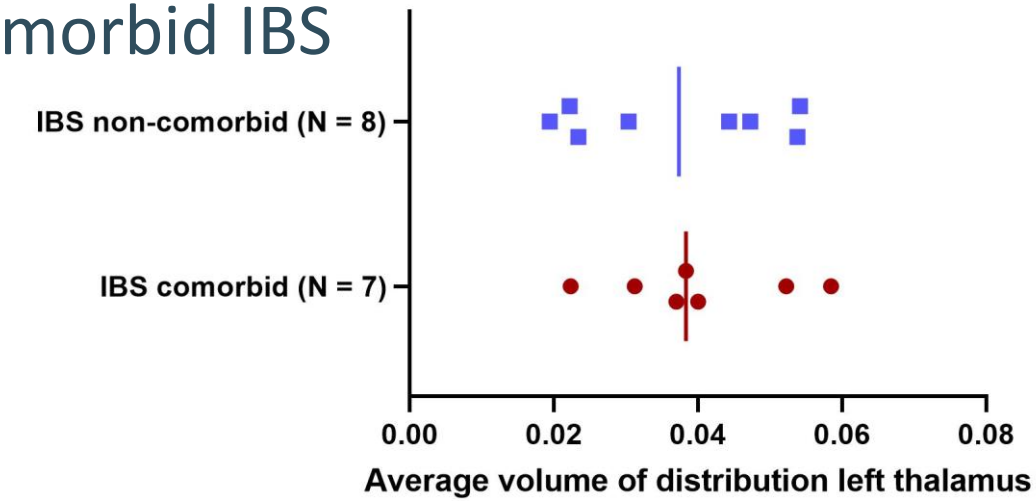
ROI analysis: no significant differences

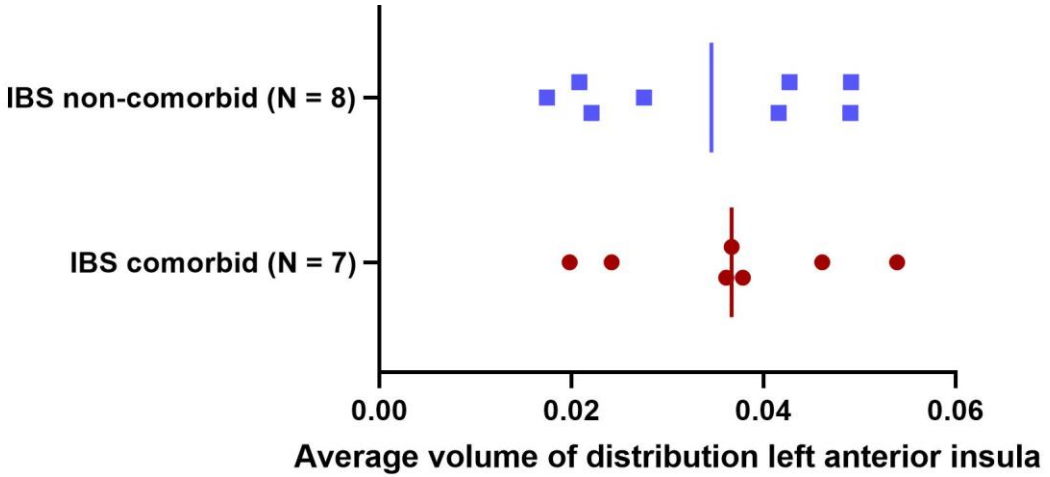
Results

2a. Neuroinflammation in comorbid vs. non-comorbid IBS



Voxel-wise analysis: no significant differences

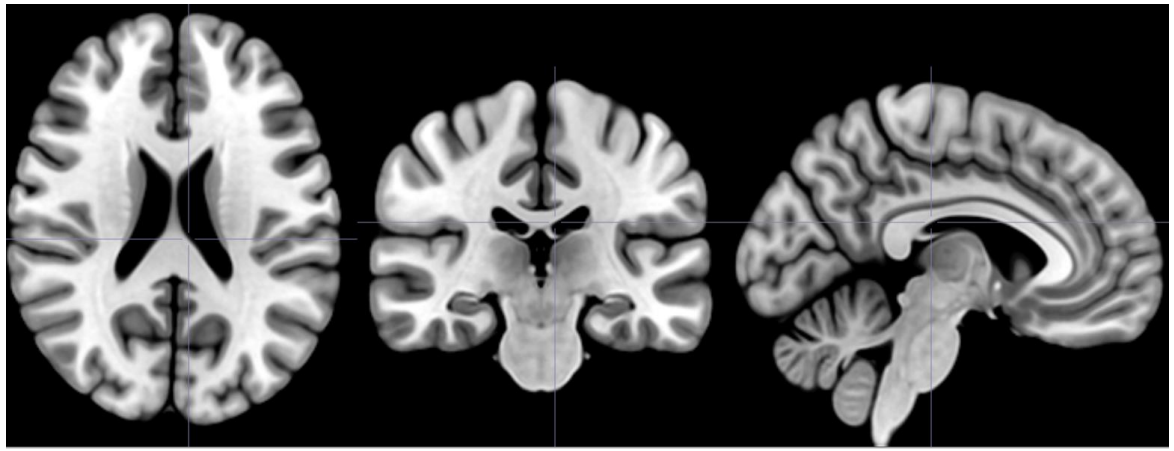




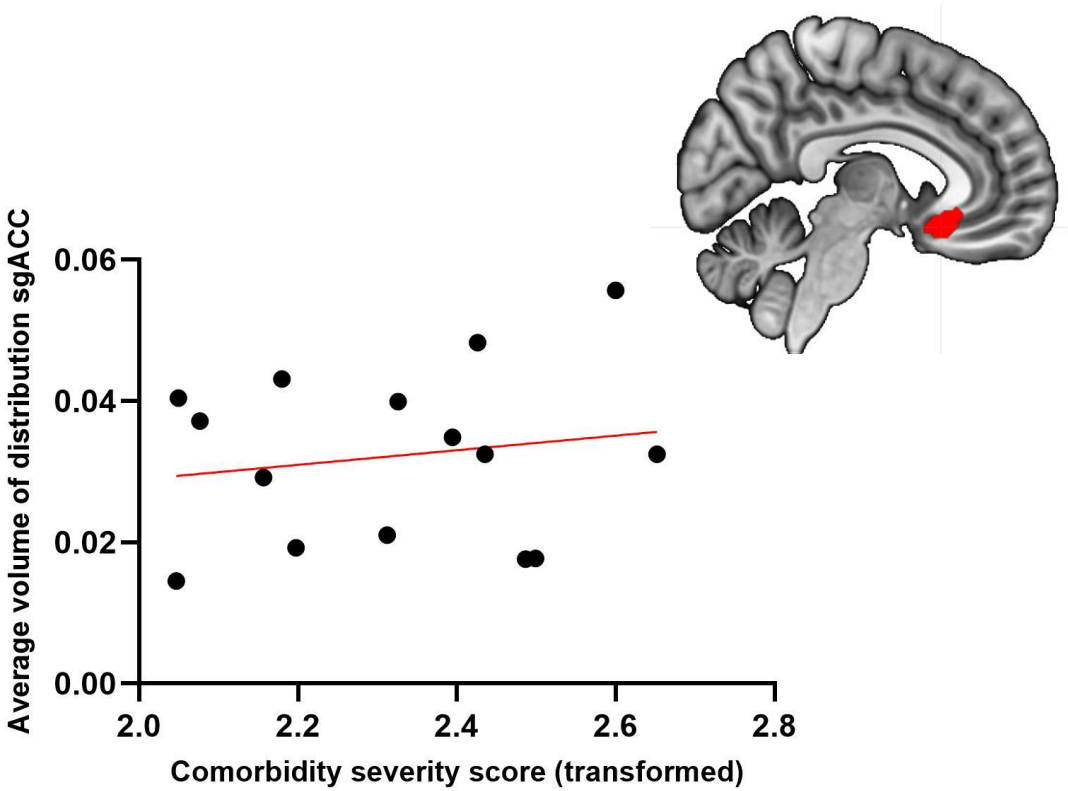
ROI analysis: no significant differences

Results

2b. Association between neuroinflammation and comorbidity composite score



Voxel-wise analysis: no significant associations



Weak association between comorbidity severity score and Vt in right sgACC (p_{uncorr} = 0.0459)

Conclusion

Our findings do not support the hypothesis of increased neuroinflammation in IBS.

Within the patient sample, neuroinflammation was not related to (the severity of) psychiatric and functional somatic comorbidities.

Thank you!

Laboratory for Brain-Gut Axis Studies

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