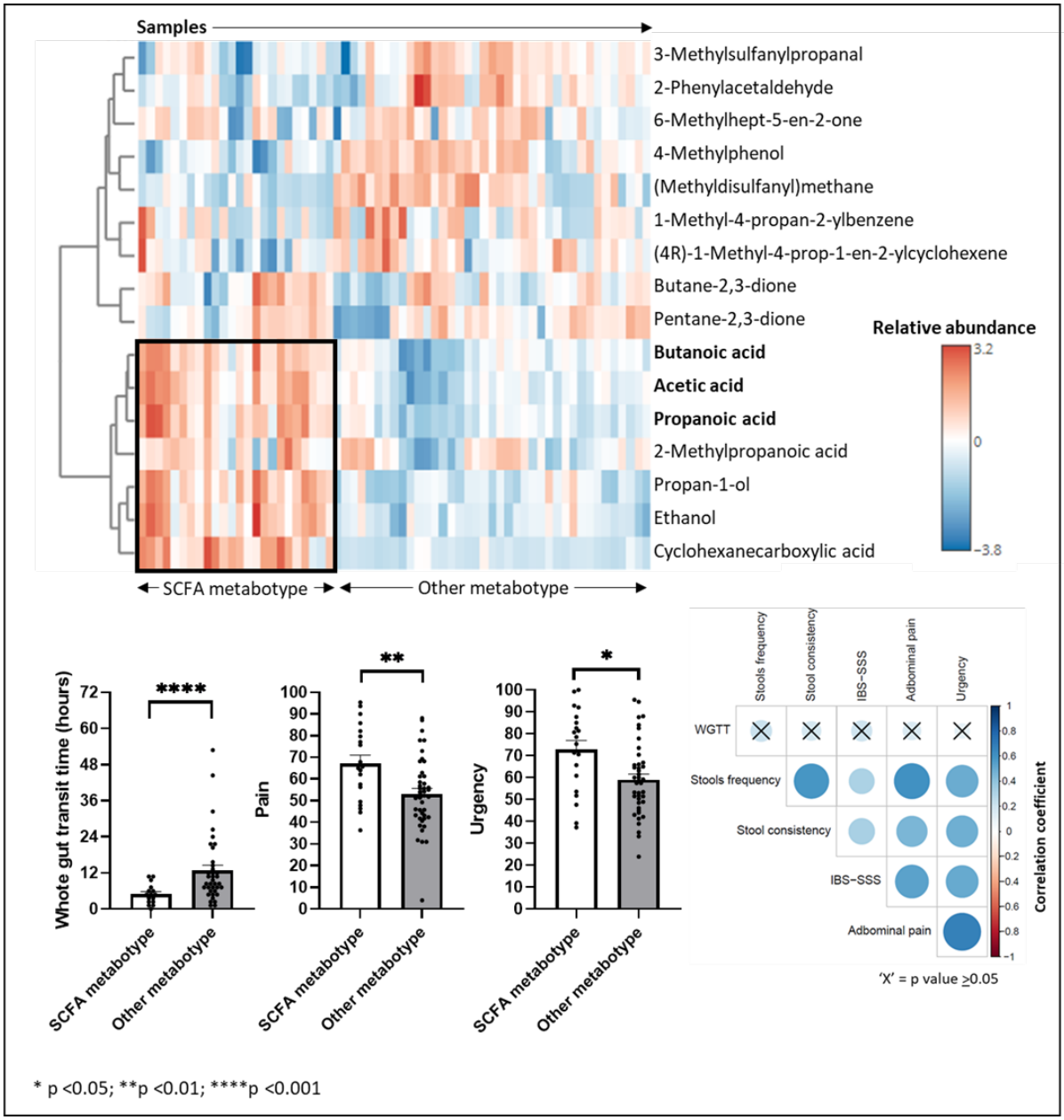
The clinical relevance of the emerging short chain fatty acid metabotype in irritable bowel syndrome

INTRODUCTION The increasing use of metabolomic analysis in irritable bowel syndrome (IBS) has led to the emergence of a distinct IBS metabotype enriched in short chain fatty acids (SCFAs). Although SCFAs are essential for gut health, there exists potential for them to exert pro-nociceptive and pro-kinetic effects depending on the colonic environment within which they are produced. Whether a metabotype rich in SCFA simply denotes a phenotype characterised by faster transit, or whether this represents a more severe IBS phenotype is uncertain.

METHODS Solid phase microextraction gas chromatography-mass spectrometry was used to examine the faecal headspace of 63 patients with moderate-severe IBS-D (diarrhoeal subtype). The SCFA metabotype was identified by hierarchical clustering - Figure 1. Baseline clinical and mechanistic data were compared between the two groups using an independent samples t-test. Clinical metrics including IBS symptom severity (IBS-SSS), abdominal pain and urgency (rating scales 0-100), stool consistency (Bristol Stool Form Scale; BSFS), and stool frequency. Mechanistic metrics included whole gut transit time (WGTT). Pearson correlation was used to detect any relationships between WGTT and symptoms in this cohort.

RESULTS The SCFA metabotype was exhibited by 32% of patients. The other metabotype was characterised by a relative deficiency of these metabolites, and a relative excess of ketones, aldehydes, and sulfoxymethanes. Patients with the SCFA metabotype were characterised by higher abdominal pain 67.2 vs 53.1; $p<0.01$) and urgency scores (72.7 vs 59.0; $p<0.05$), and greater stool frequency (4.7 vs 3.5 per 24 hours; $p<0.05$) at baseline. WGTT was significantly faster in those with the SCFA metabotype compared to those without (mean duration 5.3 vs 12.8 hours respectively; $p<0.001$, 95% CI $\mu1$-$\mu2$ [3.40-11.27]). No significant correlation was observed between WGTT and IBS symptoms.

CONCLUSION The SCFA metabotype appears to represent a more severe IBS-D phenotype characterised by pain, urgency, rapid transit and high stool frequency. Although it is possible that the enrichment of SCFA in this group could be the product of faster transit, the lack of negative-correlation between WGTT and IBS symptoms suggests that the metabolites are contributing to the generation of the more severe symptom-profile in this group.


Samples
3-Methylsulfanylpropanal
2-Phenylacetaldehyde
6-Methylhept-5-en-2-one
4-Methylphenol
(Methyldisulfanyl)methane
1-Methyl-4-propan-2-ylbenzene
(4R)-1-Methyl-4-prop-1-en-2-ylcyclohexene
Butane-2,3-dione
Pentane-2,3-dione
Butanoic acid
Acetic acid
Propanoic acid
2-Methylpropanoic acid
Propan-1-ol
Ethanol
Cyclohexanecarboxylic acid
Relative abundance
3.2
0
−3.8
SCFA metabotype
Other metabotype
Whote gut transit time (hours)
****
Pain
**
Urgency
*
SCFA metabotype
Other metabotype
Stools frequency
Stool consistency
IBS−SSS
Adbominal pain
Urgency
WGTT
Correlation coefficient
'X' = p value ≥0.05
* p <0.05; **p <0.01; ****p <0.001