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TITLE PAGE

Title: Challenging established perceptions of brain-gut interactions in functional gastrointestinal disorders: brain-gut, gut-brain, or both?

Short "running" title: FGIDs: brain-gut, gut-brain or both?

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Abbreviations:

CI	confidence interval
FD	functional dyspepsia
FGID	functional gastrointestinal disorder
HADS	hospital anxiety and depression scale
IBS	irritable bowel syndrome
OR	odds ratio

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Irritable bowel syndrome (IBS) and functional dyspepsia (FD) are functional gastrointestinal disorders (FGID) of uncertain cause. Observational studies demonstrate a high prevalence of psychological co-morbidity in FGIDs, [1-5] supporting the hypothesis that the development of these conditions is centrally mediated, via brain-gut interactions. Despite this, emerging evidence also suggests that functional bowel symptoms occurring de novo are associated with the development of anxiety or depression, implying gut-brain interactions may also exist. [6, 7]

Koloski et al. attempted to delineate the relationship between brain and gut in FGIDs in a random population sample of 2885 Australian adults. [8] At inclusion, and after a follow-up interval of 12 months, participants completed the Rome III questionnaire for IBS and FD, and the hospital anxiety and depression scale (HADS) questionnaire to assess for psychological distress. In total, 1900 (67.6%) participants completed both baseline and 12-month follow-up questionnaires. Individuals without IBS or FD, but with anxiety or depression at study entry, who went on to develop either IBS or FD subsequently were classed as having brain-gut interactions. Those with IBS or FD, but without anxiety or depression at inclusion, and who subsequently developed anxiety or depression were labelled as having gut-brain interactions.

The study demonstrated an increased odds of developing both IBS and FD with increasing anxiety severity (odds ratio (OR) per standard deviation increase in baseline HADS anxiety score = 1.31; 95% confidence interval (CI) 1.06-1.61, P = 0.01 and OR = 1.28; 95% CI 1.05-1.55, P = 0.01, respectively). There was also an increased odds of developing both IBS and FD in those with increasing depression severity (OR per standard deviation increase in baseline HADS depression score = 1.54; 95% CI 1.29-1.83, P <0.001 and OR = 1.55; 95% CI 1.32-1.83, P <0.001, respectively).

Among those with IBS, but without psychological distress at baseline, there was an increase in mean anxiety and depression scores at 12 months (mean difference in anxiety score = 0.34; 95% CI 0.13-0.55, P = 0.002 and mean difference in depression score = 0.81; 95% CI 0.47-1.15, P <0.001). A similar effect was also noted in those with pre-existing FD (mean difference in anxiety score = 0.38; 95% CI 0.14-0.63, P = 0.002 and mean difference in depression score = 0.92; 95% CI 0.57-1.27, P <0.001).

This study highlights the interplay between brain and gut and suggests that, in FGIDs, these interactions are likely to be bi-directional. Although this assertion in itself is not novel, [6] the limited follow-up of only 12 months suggests the role of brain-gut interactions is more influential and important than previously described. However, a causal link between anxiety and depression, and the development of FGIDs during longitudinal follow-up, may not be universal. Indeed, the findings of this study are in conflict with those published by the same investigators in a Scandinavian cohort of patients where anxiety, but not depression, was associated with the development of FD. [9] Although these data support the existence of a bi-directional relationship between psychological co-morbidities and FGIDs, inconsistencies in the apparent influence of psychological distress on the development, and evolution, of functional symptoms requires further longitudinal investigation.

AUTHORSHIP

Guarantor of the article: DJ Gracie

Author contributions: DJG and ACF drafted the manuscript. Both authors commented on drafts of the paper. Both authors have approved the final draft of the article.

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