An investigation of altered cortisol awakening response in females with irritable bowel syndrome

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1. Introduction

Irritable bowel syndrome (IBS) is a female-predominant stress-related gastrointestinal disorder with a high psychiatric comorbidity. Previous evidence (1) has indicated that IBS is associated with an altered cortisol awakening response. However, heterogeneity in IBS study populations may contribute to differing findings reported across research studies. It is thus currently unclear whether altered HPA axis activity is a feature of IBS *per se* or related to comorbid depression and anxiety.

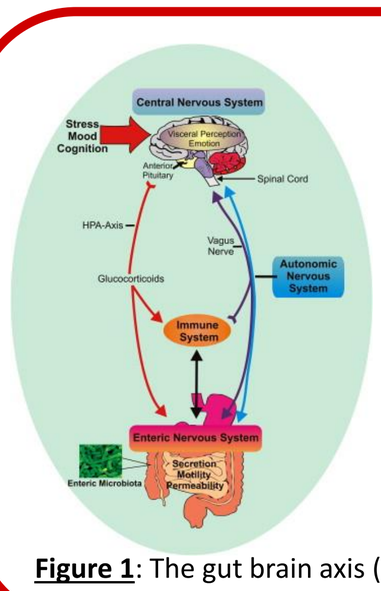

Figure 1: The gut brain axis (2)

2. Aims & Hypothesis

Aims: Assess the nature of the cortisol awakening response in a cohort of females with IBS without comorbid depression or anxiety and healthy controls.

Hypotheses: We hypothesised that females with irritable bowel syndrome would have significantly altered cortisol awakening response, that would be consistent across multiple testing days.

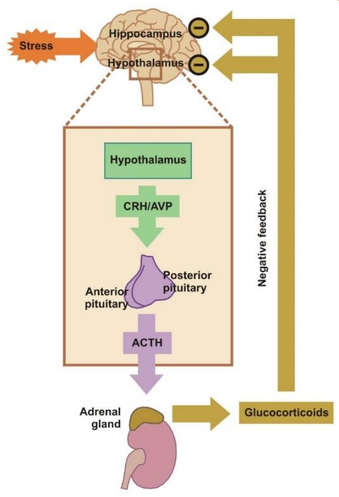

Figure 2: The HPA axis stress response (3)

3. Methods

Participants

We recruited Rome III positive IBS patients without comorbid depression or anxiety (N = 9) and healthy controls (N = 15). All participants were female. Participants were screened using the MINI International Neuropsychiatric Interview. Those who were not taking an oral contraceptive were assessed during the follicular phase of the menstrual cycle. Exclusion criteria included a formal psychiatric diagnosis of DSM-IV Axis-I Disorder (past/present); more than one first degree relative with a current or past diagnosis of MDD; use of psychoactive medications or suffering from a medical condition that could confound the aims of the study; receiving an experimental drug in previous 30 days; if premenopausal, perimenopausal, menopausal or postmenopausal; following a restricted diet regime; English not first language.

	Healthy Controls (N = 15)	IBS group (N = 9)	P-value
Age	21.5 +/- 0.5	22.8 +/- 1.3	.37
BMI	23.9+/-2.8	24.1 +/- 1.2	.73
IQ (NART)	105 +/- 1.8	104.1 +/- 2.6	.78
Education (years)	16.9 +/- 1.6	17.6 +/- 0.8	.47
IBS symptoms (IBS-SSS)	25.9 +/-7.7	142.4 +/- 18.8	< .001

Table 1: Participant characteristics. Data expressed as mean +/- SEM. BMI = body mass index. IBS-SSS = IBS symptom severity scale.
Independent samples t-tests using IBM SPSS V20.0 were used to determine group differences.

Cortisol Awakening Response

Samples were collected using Sarstedt salivettes at four time points (waking, 30 minutes, 45 minutes and 60 minutes after waking) on two mornings approximately one week apart. Salivettes were centrifuged at 1000g for 10 minutes and stored at minus 80 degrees Celsius until analysis.
Salivary cortisol was analysed using Enzo Life Sciences enzyme-linked immunosorbent assay (ELISA) kits according to manufacturer's instructions. Lower limit of detection =0.16 nmol l −1. Inter and intra-assay coefficients of variability were 11.24% and 8.2%, respectively.
Data were analysed using ANOVA of individual timepoints, as well as areas under the curve.

Figure 3: Salivette

Figure 4: Cortisol ELISA

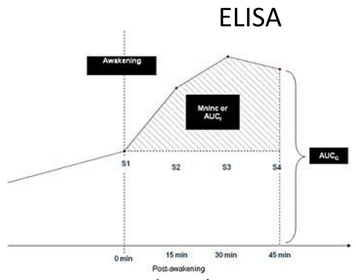

Figure 5: Area under the curve with respect to ground (AUCg) and with respect to increase (AUCi) (4)

4. Results

Cortisol Awakening Response

Cortisol levels were significantly higher post-waking at both visits (visit 1: p = .01; visit 2: p = .004). There was a slower initial rise of cortisol awakening response in IBS compared to healthy controls; this was most apparent in week 2, where IBS patients were more likely than controls to display peak cortisol levels at 45 minutes (p = .046) and less likely at 30 minutes (p = .058).

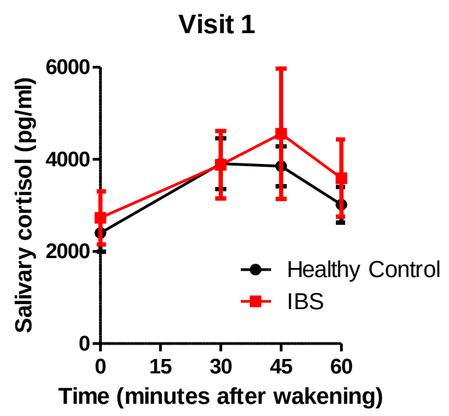

Figure 6A: Salivary waking cortisol in IBS patients and healthy controls at visit 1

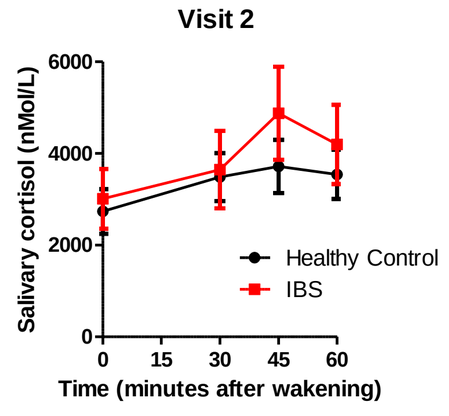

Figure 6B: Salivary waking cortisol in IBS patients and healthy controls at visit 2

In both visits, IBS patients had slightly higher AUCg (which assesses total morning cortisol output), although this was not significant (Visit 1, p = 0.71; Visit 2, p = 0.65). There was not a significant difference between IBS and healthy controls in AUCi, which assesses the change in morning cortisol output (Visit 1, p = 0.98; Visit 2, p = 0.81).

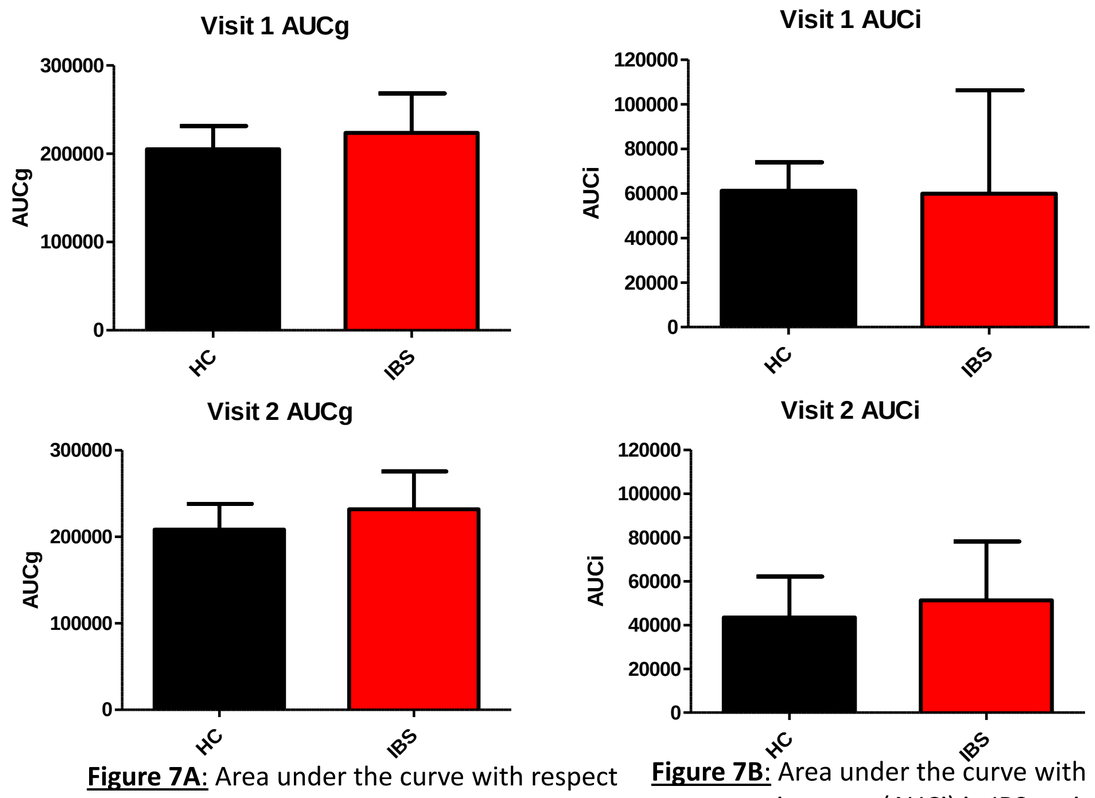

Figure 7A: Area under the curve with respect to ground (AUCg) in IBS patients and healthy controls

Figure 7B: Area under the curve with respect to increase (AUCi) in IBS patients and healthy controls

5. Discussion & conclusions

- Although overall cortisol output was not significantly different in IBS patients, the profile of their cortisol awakening response was altered, with cortisol peaking later post-awakening.
- The current results offer further evidence of altered HPA axis activity in irritable bowel syndrome; further research is required into the nature and stability of these changes over time.

6. Acknowledgements & Disclosure

The APC Microbiome Institute is a research centre funded by Science Foundation Ireland (SFI), through the Irish Government's National Development Plan. The authors and their work were supported by SFI (grant numbers SFI/12/RC/2273), by the Health Research Board (HRB) through Health Research Awards (grants no HRA_POR/2011/23; TGD, JFC and GC, HRA_POR/2012/32; HRA-POR-2-14-647: GC, TGD, PK, ANC, DWM), by the Health Service Executive (HSE HaPAI/2015/GC), and through EU GRANT 613979 (MYNEWGUT FP7-KBBE-2013-7: TGD, JFC). The Centre has conducted studies in collaboration with several companies including GSK, Pfizer, Wyeth and Mead Johnson. GC is supported by a NARSAD Young Investigator Grant from the Brain and Behavior Research Foundation (Grant Number 20771).

7. References

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