Supporting documents: Table A. Basal and stimulated levels of HPA axis hormones in IBS

Study	Diagnosis (n)	Stimulus	Source	Time of collection	ACTH levels (IBS vs. Controls)	Cortisol levels (IBS vs. Controls)
Basal levels						
Heitkemper 1996[82]	IBS (24) IBS non-patients (24) Controls (25)	NA	urine	am and pm	-	Trend for ↑
Patacchioli 2001[63]	IBS (55) Controls (28)	NA	saliva	am and pm	-	↑
Bohmelt 2005[64]	IBS/NUD (30) Controls (24)	NA	saliva	8am, 11am, 3pm, 8pm	-	↓
Burr NGM 2009[65]	IBS (30) Controls (31)	NA	blood	q20min, 8pm to awake	-	↑ in IBS-C
Chang 2009[60]	IBS (24) IBS+FM (16) Controls (25)	NA	blood	q10min x 24 hrs	↓	↑
Hormone challenge						
Bohmelt 2005[64]	IBS/NUD (30) Controls (24)	CRF	blood saliva	Baseline and 20, 30, 45, 60, 90 and 120 min after CRF	↓	↓
Dinan 2006[62]	IBS (21) Controls (21)	CRF	blood	Baseline and immediately and 15, 30, 45, 60, 90, and 120 minutes after CRF	↑	↑
Fukudo 1998[38]	IBS (10) Controls (10)	CRF	blood	Standard collection	↑	No difference

Meal and/or mental stressor						
Elsenbruch 2001[66]	IBS (24) Controls (20)	Standard meal	saliva	Baseline x2, immediately and 30 and 60 min after meal	-	↑ IBS-D/A post-meal vs. baseline but no group difference
Elsenbruch 2001[32]	IBS (24) Controls (20)	Standard meal+ Modified Stroop test	saliva	Baseline x 2, immediately after meal, after stressor/rest period, after recovery period	-	No difference
Walter 2006[83]	IBS (27) Functional constipation (13) Controls (18)	Liquid meal + rectal distensions	saliva	8am, 1pm, 3pm, 10pm on day without stressor and day of stressor	-	No difference
Elsenbruch 2004[69]	IBS (15) Controls (15)	Liquid nutrient load	blood	Baseline, immediately and 15, 45, 75, 105 min after meal	-	No difference
Elsenbruch 2006[59]	IBS (17) Controls (12)	Public speaking	blood	Baseline and immediately and 45 min after stressor	No difference	No difference
Posserud 2004[33]	IBS (18) Controls (22)	Mental stress + rectal distensions	blood	After distension only and after stress+distension	↑ CRF and ACTH in IBS and not controls; no group difference	No difference
Physical stressor						
Videlock 2009[61]	IBS (44) Controls (39)	Sigmoidoscopy	saliva	Baseline and immediately and 10, 20, 30, 45, and 60 min after stressor	-	No difference

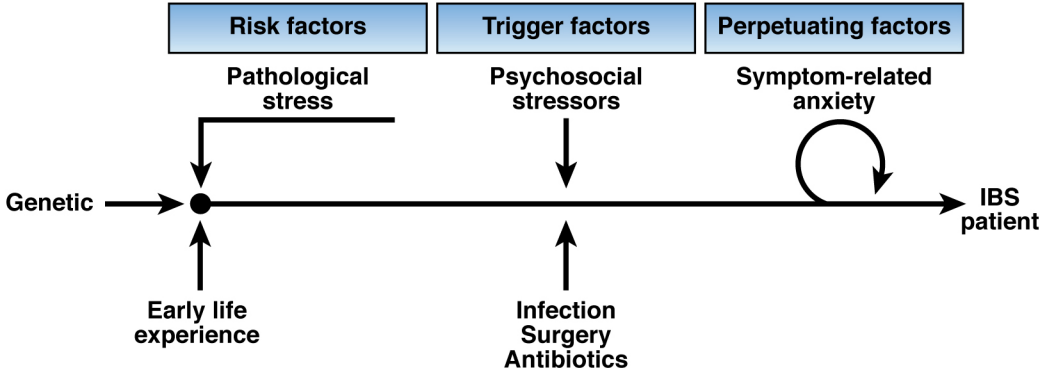
FitzGerald 2009[68]	IBS-D (F, 13) Controls (F, 13)	Lumbar puncture	blood saliva		↓	↓
Zhou 2010[67]	IBS-D (78) Controls (57)	Ischemic arm test	blood	Baseline, immediately after stressor, 60 min after stressor	↑	↑
Zhou 2010[67]	IBS-D (78) Controls (57)	Thermal, mechanical, & cold preesor	blood	Baseline, immediately after stressor, 60 min after stressor	No difference	No difference

Abbreviations: FM = Fibromyalgia; NUD = non-ulcer dyspepsia

Supporting documents

Figure A. Role of stress in development and modulation of irritable bowel syndrome (IBS) symptoms.[5] Different types of stressors may play a role in the permanent biasing of stress responsiveness, the transient activation of the stress response, the increased vulnerability of developing IBS, and the persistence of symptoms.

Figure B. The stress system.[85] The HPA axis has been studied extensively in the stress response. Neurons in the medial parvocellular region of the PVN of the hypothalamus release CRH and arginine vasopressin (AVP). This then triggers the secretion of ACTH from the pituitary gland, subsequently leading to the production of glucocorticoids by the adrenal cortex. The stress-induced responsiveness of the HPA axis is in part modulated by the ability of glucocorticoids to regulate ACTH and CRF release by binding to two corticosteroid receptors, the glucocorticoid receptor (GR) and the mineralocorticoid receptor (MR) which are part of the feedback loop. Under normal physiologic conditions, after the HPA axis is activated and the stressor is perceived to have subsided, these feedback loops are triggered at various levels of the system in order to shut down the HPA axis and return to a set homeostatic point. However, the amygdala has a feed forward mechanism to activate the HPA axis during stress to deal with the challenge.


Risk factors
Trigger factors
Perpetuating factors
Pathological stress
Psychosocial stressors
Symptom-related anxiety
Genetic
IBS patient
Early life experience
Infection
Surgery
Antibiotics