



I disturbi funzionali: il corpo e la mente

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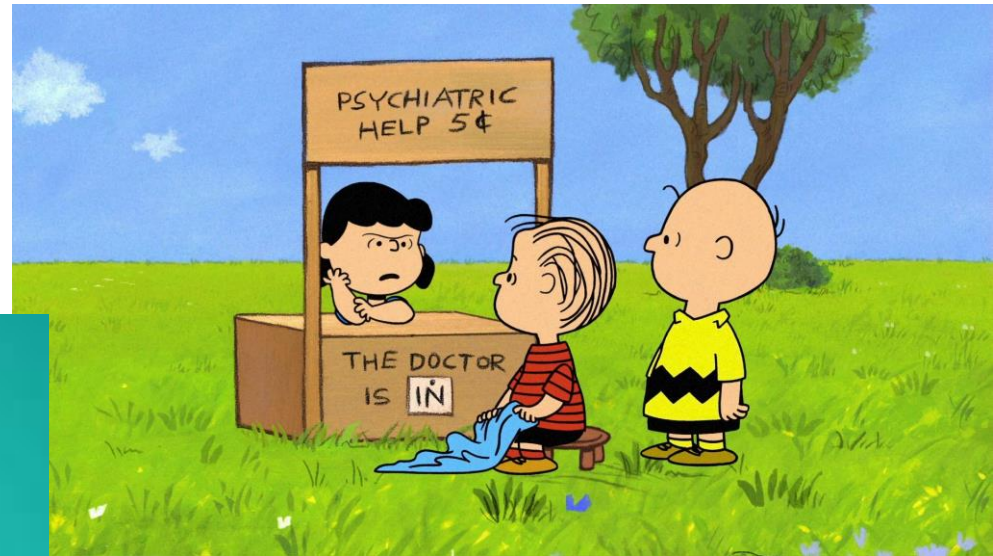
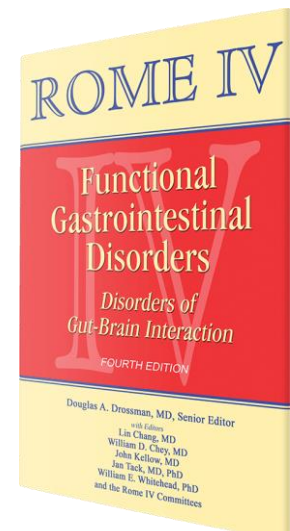


Table 2. Functional Gastrointestinal Disorders: Disorders of Gut–Brain Interaction

A. Esophageal Disorders	
A1. Functional chest pain	A4. Globus
A2. Functional heartburn	A5. Functional dysphagia
A3. Reflux hypersensitivity	
B. Gastroduodenal Disorders	
B1. Functional dyspepsia	B3. Nausea and vomiting disorders
B1a. Postprandial distress syndrome (PDS)	B3a. Chronic nausea vomiting syndrome (CNVS)
B1b. Epigastric pain syndrome (EPS)	B3b. Cyclic vomiting syndrome (CVS)
B2. Belching disorders	B3c. Cannabinoid hyperemesis syndrome (CHS)
B2a. Excessive supragastric belching	B4. Rumination syndrome
B2b. Excessive gastric belching	
C. Bowel Disorders	
C1. Irritable bowel syndrome (IBS)	C2. Functional constipation
IBS with predominant constipation (IBS-C)	C3. Functional diarrhea
IBS with predominant diarrhea (IBS-D)	C4. Functional abdominal bloating/distension
IBS with mixed bowel habits (IBS-M)	C5. Unspecified functional bowel disorder
IBS unclassified (IBS-U)	C6. Opioid-induced constipation
D. Centrally Mediated Disorders of Gastrointestinal Pain	
D1. Centrally mediated abdominal pain syndrome (CAPS)	
D2. Narcotic bowel syndrome (NBS)/ Opioid-induced GI hyperalgesia	
E. Gallbladder and Sphincter of Oddi (SO) Disorders	
E1. Biliary pain	
E1a. Functional gallbladder disorder	
E1b. Functional biliary SO disorder	
E2. Functional pancreatic SO disorder	
F. Anorectal Disorders	
F1. Fecal incontinence	F2c. Proctalgia fugax
F2. Functional anorectal pain	F3. Functional defecation disorders
F2a. Levator ani syndrome	F3a. Inadequate defecatory propulsion
F2b. Unspecified functional anorectal pain	F3b. Dyssynergic defecation
G. Childhood Functional GI Disorders: Neonate/Toddler	
G1. Infant regurgitation	G5. Functional diarrhea
G2. Rumination syndrome	G6. Infant dyschezia
G3. Cyclic vomiting syndrome (CVS)	G7. Functional constipation
G4. Infant colic	
H. Childhood Functional GI Disorders: Child/Adolescent	
H1. Functional nausea and vomiting disorders	H2a1. Postprandial distress syndrome
H1a. Cyclic vomiting syndrome (CVS)	H2a2. Epigastric pain syndrome
H1b. Functional nausea and functional vomiting	H2b. Irritable bowel syndrome (IBS)
	H2c. Abdominal migraine
H1b1. Functional nausea	H2d. Functional abdominal pain – NOS
H1b2. Functional vomiting	H3. Functional defecation disorders
H1c. Rumination syndrome	H3a. Functional constipation
H1d. Aerophagia	H3b. Nonretentive fecal incontinence
H2. Functional abdominal pain disorders	
H2a. Functional dyspepsia	



The complex interplay between gastrointestinal and psychiatric symptoms in irritable bowel syndrome: A longitudinal assessment

Journal of Gastroenterology and Hepatology 34 (2019) 713–719

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Psychological distress is an important **risk factor** for the **development of FGIDs** and, when present, can perpetuate or **exacerbate** symptoms. Further, it affects the **doctor patient relationship** and negatively impacts **treatment outcomes**.

Comorbid anxiety and depression are independent predictors of post-infectious IBS and functional dyspepsia (FD)

However, **psychological distress can also be a consequence**, rather than a cause, of disease burden.

(Van Oudenhove L, 2016)

(Zamani, 2019)

Anxiety disorders occur in 30- 50% of **FGID** patients.

They may **initiate or perpetuate** FGID symptoms through **heightened autonomic arousal** in response to stress, which can interfere with GI sensitivity and motor function.

(Van Oudenhove L, 2016)

Overlap between **depression** and **FGID** is about **30% in primary care** settings and slightly **higher in tertiary care**.

Depression can impact the **number of functional GI** symptoms.

Comorbid depression has been linked to **poor outcomes, high health care utilization and cost, functional impairment, poor quality of life.**

Suicidal ideation is present in between 15% and 38% of IBS pts. linked to hopelessness associated with symptom severity, interference with life, and inadequacy of treatment.



Systematic review with meta-analysis: the prevalence of anxiety and depression in patients with irritable bowel syndrome

Mohammad Zamani^{1,2} | Shaghayegh Alizadeh-Tabari¹ | Vahid Zamani³

Aliment Pharmacol Ther. 2019;50:132-143.

(73 studies).

**Perfino le mie ansie
hanno l'ansia.**



Prevalence rates of **anxiety** symptoms and disorders in IBS patients were 39.1% and 23%, respectively

Prevalence of **depressive** symptoms and disorders in IBS patients was 28.8% and 23.3%, respectively

A higher prevalence of anxiety and depressive symptoms in **female** individuals than in male individuals.

IBS patients with high levels of **anxiety** were mostly those with **IBS-C** and **IBS-D**, while **depression** was associated only to **IBS-D**.

IBS clinical management in Italy: The AIGO survey[☆]

Marco Soncini^a, Cristina Stasi^{b,*}, Paolo Usai Satta^c, Giuseppe Milazzo^d,
Margherita Bianco^e, Gioacchino Leandro^e, Luigi Maria Montalbano^f, Nicola Muscatiello^g,
Fabio Monica^h, Francesca Galeazziⁱ, Massimo Bellini^j, on behalf of the AIGO¹

Digestive and Liver Disease 51 (2019) 782–789

HADS and SF according to gender			
	Sex		p
	Female (N = 493)	Male (N = 184)	
Physical Component Summary — PSC-12 (M ± SD)	43.9 ± 9.1	45.2 ± 8.1	0.12 ^b
Mental Component Summary — MCS-12 (M ± SD)	39.0 ± 11.0	41.7 ± 10.1	0.005 ^b
HADS — anxiety (%)			0.007 ^a
0–7 (Normal)	172– (34.9)	86+ (46.7)	
8–10 (Borderline)	130 (26.4)	48 (26.1)	
≥11 (Pathological)	191+ (38.7)	50– (27.2)	
HADS — depression (%)			0.013 ^a
0–7 (Normal)	288– (58.4)	124+ (67.4)	
8–10 (Borderline)	122 (24.7)	45 (24.5)	
≥11 (Pathological)	83+ (16.8)	15– (8.2)	
Requested diagnostic test (%)			0.14 ^a
No	66 (13.4)	33 (17.9)	
Yes	427 (86.6)	151 (82.1)	
Suggested therapies (%)			0.49 ^a
No	31 (6.3)	9 (4.9)	
Yes	462 (93.7)	175 (95.1)	

Anxious pathological state in >1/3 of the pts.;
Depressive pathological state in 14.5% of pts.

Both anxiety (38.7%) and depression (16.8%) levels higher in **females**

The **mental** component of **SF 12** was lower in females

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HADS and SF according to severity of IBS symptoms					
	IBS-SSS				p
	Normal N (%)	Mild N (%)	Moderate N (%)	Severe N (%)	
HADS – anxiety (%)					<0.001 ^a
0–7 (Normal)	4 (100)	50 ⁺ (58.8)	162 ⁺ (49.2)	42 [–] (16.2)	
8–10 (Borderline)	0	24 (28.1)	95 (28.9)	59 (22.8)	
≥11 (Pathological)	0	11 [–] (12.9)	72 [–] (21.9)	158 ⁺ (61)	
HADS – depression (%)					<0.001 ^a
0–7 (Normal)	4 (100)	53 (62.4)	240 ⁺ (72.9)	115 [–] (44.4)	
8–10 (Borderline)	0	27 (31.8)	64 [–] (19.5)	76 (29.3)	
≥11 (Pathological)	0	5 (5.9)	25 [–] (7.6)	68 ⁺ (26.3)	
Requested diagnostic test (%)					0.16 ^a
No	0	19 (22.4)	45 (13.7)	35 (13.5)	
Yes	4 (100)	66 (77.6)	284 (86.3)	224 (86.5)	0.13 ^a
Suggested therapies (%)					
No	0	9 (10.6)	21 (6.4)	10 (3.9)	<0.001 ^a
Yes	4 (100)	76 (89.4)	308 (93.6)	249 (96.1)	
Sex (%)					<0.001 ^a
Female	2 (50)	52 (61.2)	228 (69.3)	211 (81.5)	
Male	2 (50)	33 (38.8)	101 (30.7)	48 (18.5)	<0.001 ^c
Physical Component Summary – PSC-12 (M ± SD)	53.6 ± 2.3	50.0 ± 6.9	46.3 ± 7.8	39.5 ± 8.6	
Mental Component Summary – MCS-12 (M ± SD)	48.7 ± 6.1	44.5 ± 9.8	42.7 ± 9.4	34.2 ± 10.5	<0.001 ^c
Age (M ± SD)	52.5 ± 4.7	45.3 ± 16.2	44.0 ± 15.3	41.0 ± 14.9	

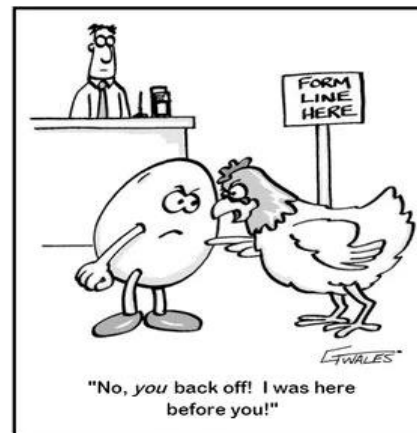
^a/– Observed frequencies greater (+) than or less (–) than chance (adjusted residual analysis).

-**HADS**, request for diagnostic tests and therapy prescription increased with symptom severity.

-SF 12, both physical and mental components, decreased with increase in IBS-SSS.



In patients with FGID and mood disturbances, the gut symptoms precede mood disorder in **2/3** of cases.



A third of patients develop mood disorders before the onset of gut symptoms.

Mood and Anxiety Disorders Precede Development of Functional Gastrointestinal Disorders in Patients but Not in the Population



Michael P. Jones,^{*} Jan Tack,[‡] Lukas Van Oudenhove,^{‡,§} Marjorie M. Walker,^{||}
Gerald Holtmann,^{||} Natasha A. Koloski,^{||,¶} and Nicholas J. Talley^{||}

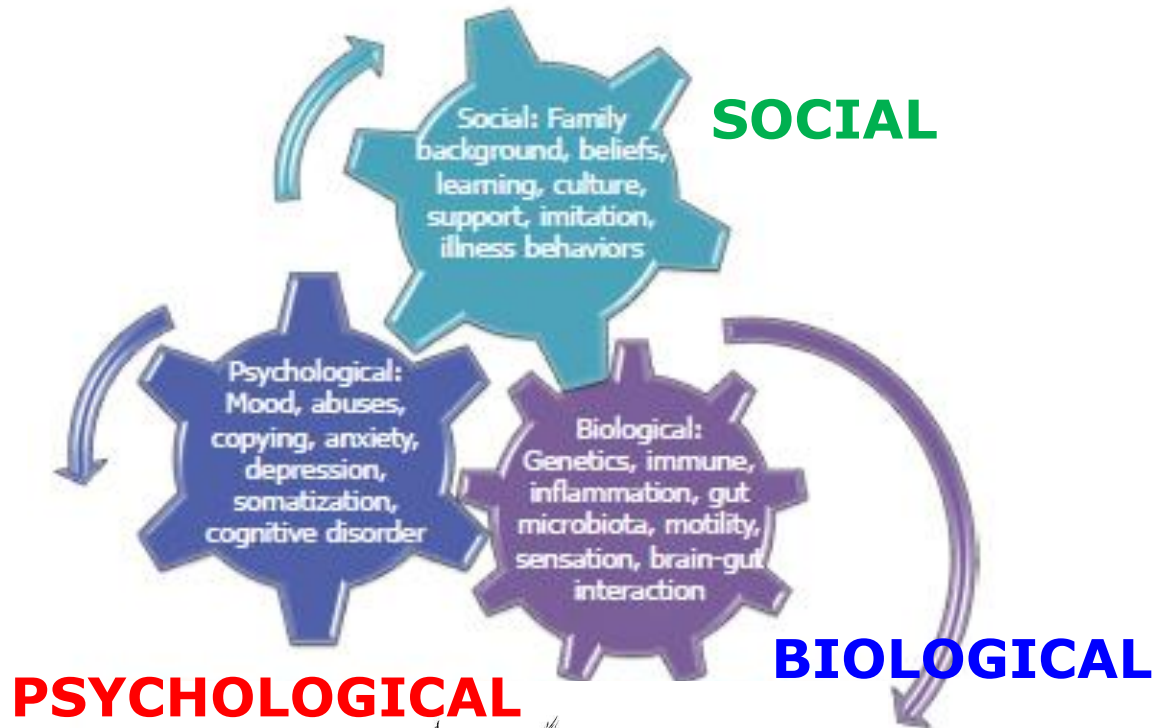
Clinical Gastroenterology and Hepatology 2017;15:1014–1020

Among the 4966 health care seekers, 3279 patients were diagnosed with a **mood or anxiety disorder before** an FGID (ratio of **2:1**).



Among patients, the **mood or anxiety disorder** was on average diagnosed **> 3 years before the FGID**.

The **biopsychosocial model** is not only confined to the **FGIDs** but also adopted in many pain related disorders such as **migraine**, **tension headache**, **chronic fatigue syndrome**, and **fibromyalgia**. A concept of **central sensitivity syndromes** (dysregulated nociception) is proposed to unite these comorbidities that share the same biopsychosocial dysfunction *(Chang FY, 2014)*

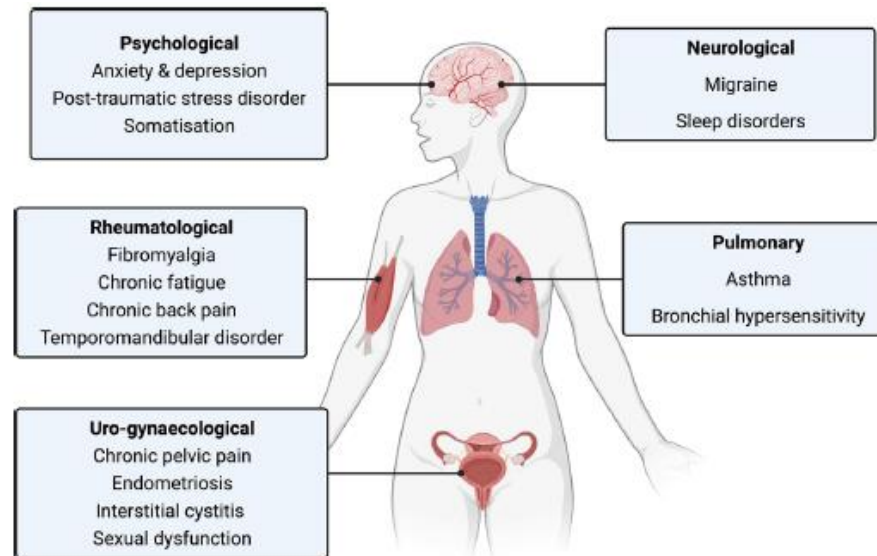


Common extraintestinal comorbidities of FGID



SOMATIZATION (2/3 of FGID pts.)

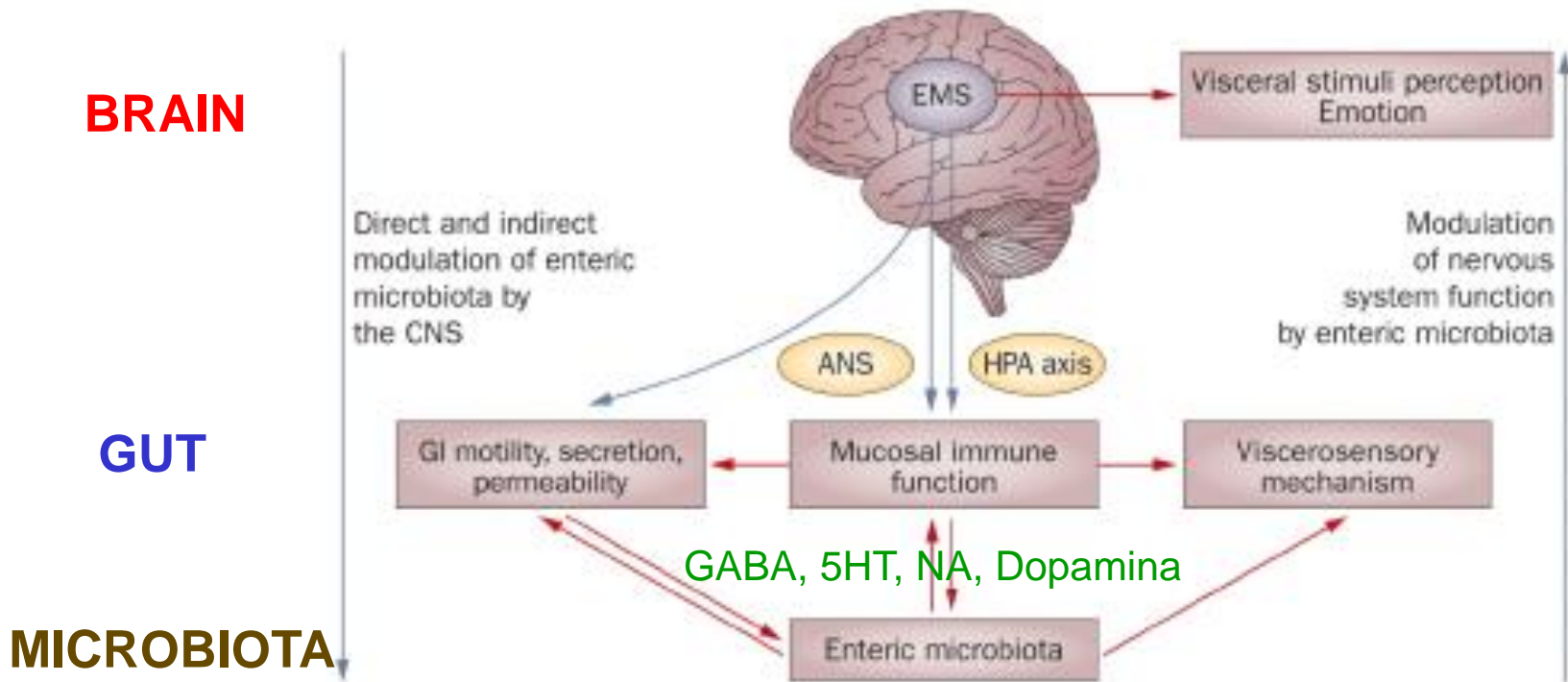
(Shiha G, 2021)



(Van Oudenhove L, 2016)

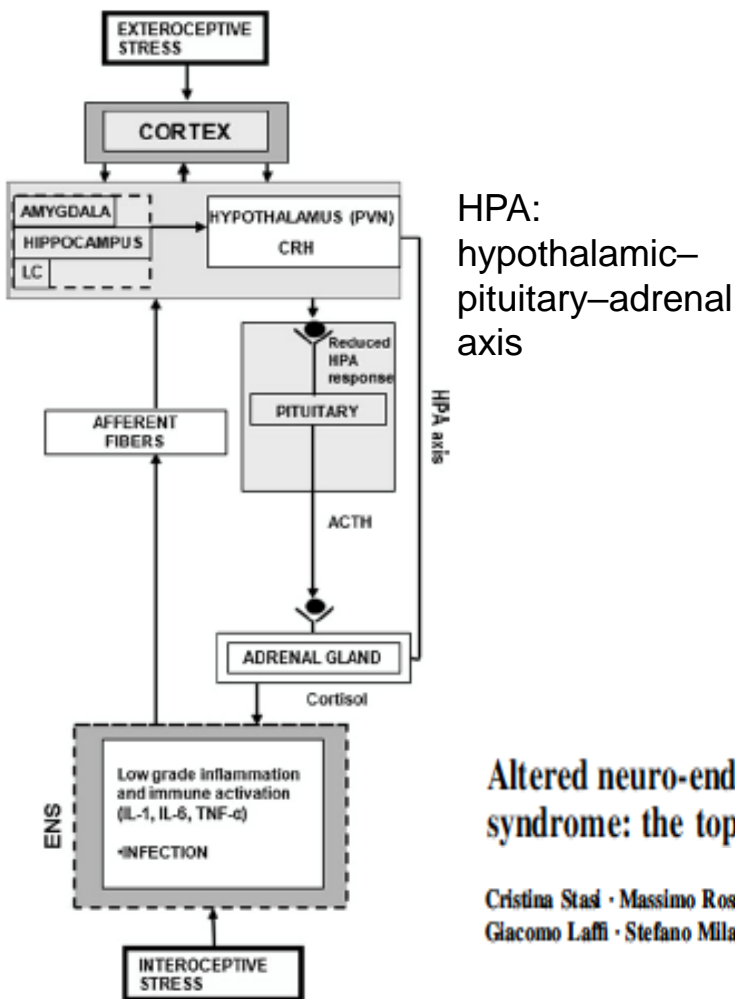
Somatization associated with

- increased frequency** and **severity** of abdominal **pain**,
- reduced **productivity**,
- increased **healthcare utilisation** (inappropriate **investigations**, excess **medication** use and unnecessary **surgical** interventions) and **costs**
- increased psychological distress**, patient **dissatisfaction**



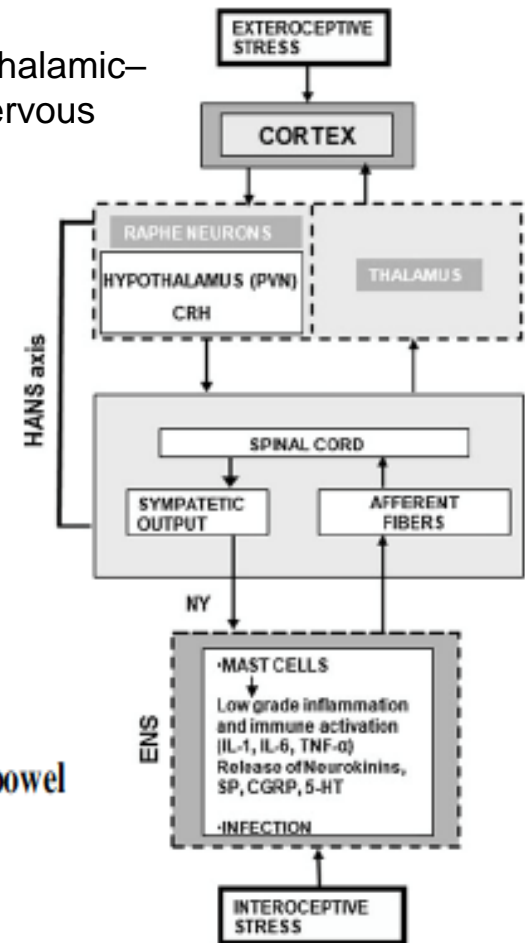
Bidirectional interactions between brain and enteric microbes might have an important role in modulating gut function and may be involved in the modulation of **emotions, pain perception and general well-being**.

FGID symptoms may be caused either by alterations in the **CNS** (top-down model), or in the **periphery** (bottom-up model), or in a **combination** of both. The brain–gut axis may be stimulated by various stressors either directed to the CNS (exteroceptive stress) or to the gut (interoceptive stress).



HPA:
hypothalamic–
pituitary–adrenal
axis

HANS: hypothalamic–
autonomic nervous
system axis



Altered neuro-endocrine-immune pathways in the irritable bowel syndrome: the top-down and the bottom-up model

Cristina Stasi · Massimo Roselli · Massimo Bellini ·
Giacomo Laffi · Stefano Milani

J Gastroenterol
DOI 10.1007/s00535-012-0627-7

Under **normal** physiological conditions, most of **interoceptive** gut brain **signals** are **not consciously perceived** because visceral afferent input is processed and continuously modulated by cognitive and affective circuits at the level of the **brain** and through **descending modulatory pathways**.

Van Oudenhove L, 2016

Altered visceral sensation in **IBS** is characterised by **central abnormalities** in sensory, emotional arousal, and prefrontal **cortical regions** of the brain.

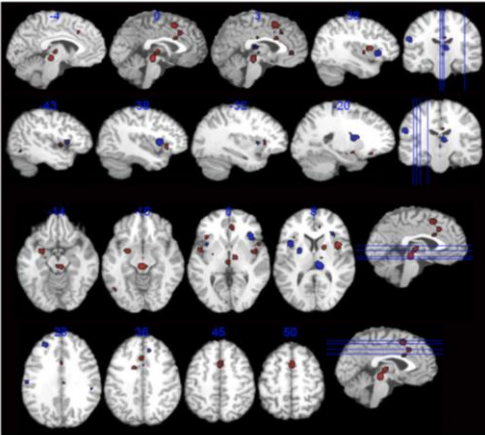
Alterations in the **descending pathways modulating sensation** and peripheral mechanisms are also involved in the pathogenesis of visceral pain allowing physiological (non-noxious) stimuli to be perceived as painful or unpleasant (**allodynia / visceral hypersensitivity**)

(Ford A, 2019)

Quantitative Meta-analysis Identifies Brain Regions Activated During Rectal Distension in Irritable Bowel Syndrome

KIRSTEN TILLISCH, EMERAN A. MAYER, and JENNIFER S. LABUS

Center for Neurobiology of Stress, Departments of Medicine, Physiology and Biobehavioral Sciences, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California



Neuroimaging studies: **changes in specific brain regions** in patients with IBS, involved in the processing of emotions, cognition, memory and autonomic functioning
(Weaver KR, 2016)

Patients with IBS have greater engagement of **regions involved in emotional arousal** network.

Measures of regional cerebral blood flow during rectal distention have shown that IBS patients have **greater activation** of the anterior cingulate cortex, amygdala and dorsomedial frontal cortex, in contrast to patients with ulcerative colitis and controls
Mayer EA et al., *Pain*, 2005

The antidepressant **amitriptyline** has been shown to **reduce rectal pain** and this has been **correlated to activation** of the right prefrontal cortex, right insula and perigenual anterior cingulate cortex.
Morgan V et al., *Gut*, 2005

We recommend that TCAs be used to treat global symptoms of IBS.
Strong recommendation; moderate quality of evidence.

12 RCTs: IBS pts. randomized to a TCA were more likely to note improvement in **global IBS symptoms** compared with those randomized to placebo.

Of patients who received active therapy, 42.7% did not improve compared with 63.8% of those randomized to placebo who did not improve.

The **NNT** with TCAs was **4.5**

Patients should be started on a low dose (e.g., 10-mg amitriptyline or 10 mg of desipramine) with gradual dose titration upward to achieve therapeutic relief of symptoms while minimizing side effects

ACG Clinical Guideline: Management of Irritable Bowel Syndrome

Am J Gastroenterol 2021;116:17-44.

We suggest that gut-directed psychotherapies be used to treat global IBS symptoms.

Conditional recommendations; very low quality of evidence.

Gut Directed Psychotherapies (GDPs) **in conjunction** with other IBS therapies for patients who are emotionally stable but who exhibit cognitive-affective drivers of IBS symptoms because

- low risk when used by **qualified health professionals**
- long-term benefits of these therapies even after they are discontinued;

GDPs are independent from IBS subtype

NNT collectively remains 4 when the validated IBS-SSS is used as a primary outcome measure

Tricyclic antidepressants are an effective **second-line** drug for **global symptoms and abdominal pain** in IBS.

They can be initiated in primary or secondary care, but **careful explanation** as to the rationale for their use is required, and patients should be counselled about their side-effect profile. They should be commenced at a low dose (eg, 10 mg amitriptyline once a day) and titrated slowly to a maximum of 30–50 mg once a day (***recommendation: strong, quality of evidence: moderate***).

Selective serotonin reuptake inhibitors may be an effective **second-line** drug for **global symptoms** in IBS. They can be initiated in primary or secondary care, but **careful explanation** as to the rationale for their use is required, and patients should be counselled about their side-effect profile (***recommendation: weak, quality of evidence: low***).

Psychological therapies

-IBS-specific **cognitive behavioural therapy** may be an efficacious treatment for global symptoms in IBS

(recommendation: strong, quality of evidence: low).

-Gut-directed **hypnotherapy** may be an efficacious treatment for global symptoms in IBS

(recommendation: strong, quality of evidence: low).

-**Psychological therapies** should be considered when symptoms have not improved after 12 months of drug treatment.

Referral can be made at an **earlier** stage, **if accessible locally**, and based **on patient preference**

(recommendation: strong, quality of evidence: low).

Psychological/psychiatric interventions: depending on the availability of appropriate resources and expertise

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Marco Soncini^a, Cristina Stasi^{b,*}, Paolo Usai Satta^c, Giuseppe Milazzo^d,
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Digestive and Liver Disease 51 (2019) 782–789

Therapies suggested by gastroenterologists in the different IBS subgroups.

	IBS IBS-C (N = 294)	IBS-D (N = 146)	IBS-M (N = 237)	p
None	16 (5.4)	6 (4.1)	17 (7.2)	ns
Life style and dietary suggestions	210 (71.4)	107 (73.3)	162 (68.4)	ns
Probiotics	125 ⁻ (42.5)	86 ⁺ (58.9)	129 (54.4)	<0.01
Fiber supplements	69 ⁺ (23.5)	9 ⁻ (6.2)	32 (13.5)	<0.001
Antispasmodics	13 ⁻ (4.4)	15 (10.3)	27 ⁺ (11.4)	<0.01
Stimulant laxatives	4 (1.4)	1 (0.7)	0	ns
Macrogol	146 ⁺ (49.7)	6 ⁻ (4.1)	31 ⁻ (13.1)	<0.001
Lactulose/lactitole	7 (2.4)	1 (0.7)	2 (0.8)	ns
Saline laxatives	2 (0.7)	1 (0.7)	2 (0.8)	ns
Enemas/suppositories/micro-enemas	12 ⁺ (4.1)	1 (0.7)	2 (0.8)	<0.05
Prucalopride	9 ⁺ (3.1)	0	0 ⁻	<0.05
Linacotide	25 ⁺ (8.5)	1 ⁻ (0.7)	5 ⁻ (2.1)	<0.001
Rifaximine	6 ⁻ (2.0)	12 ⁺ (8.2)	13 (5.5)	0.01
Mesalamine	9 (3.1)	6 (4.1)	3 (1.3)	ns
Herbal remedies	6 (2.0)	4 (2.7)	9 (3.8)	ns
→ Psychotherapy	44 (15.0)	19 (13.0)	29 (12.2)	ns
→ Antidepressant drugs (TCA/SSRI)	0 (0.0)	0 (0.0)	1 (0.4)	ns
Loperamide	0 (0.0)	18 (12.3)	7 (2.9)	<0.001
Other	41 (13.9)	14 (9.6)	28 (11.8)	ns

+/- Observed frequencies greater (+) than or less (-) than chance (adjusted residual analysis).





Should IBS patients be assessed for psychological comorbidities?

We recommend **FOR** psychological comorbidities assessment in IBS patients.

Consensus recommendation; unable to assess using GRADE methodology.

Who, When and Why?

**Irritable bowel syndrome in adults in primary care:
summary of updated NICE guidance**

BMJ 2015;350:h701

Cheryl Hookway *technical analyst*¹, Sara Buckner *technical analyst*², Paul Crosland *health economist*², Damien Longson *consultant liaison psychiatrist*³

Consider referral for psychological interventions (cognitive behavioural therapy (CBT), hypnotherapy, or psychological therapy (or a combination)) in people who do **not respond to drug treatments after 12 months** and who develop a continuing symptom profile (described as **refractory IBS**).

NASCONO GLI JUVENTINI NEGAZIONISTI



GUIDELINES AND FLAG

Consider involvement

Question	Answer
1. Question for anxiety: In the last week, have you felt tense or wound up?	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>
2. Question for depression: In the last week, have you felt downhearted and low?	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>
3. Question for suicidal ideation: Have you recently felt so low that you felt like hurting or killing yourself?	<input type="radio"/> <input type="radio"/> <input type="radio"/>

GUIDELINES AND FLAGS FOR

Consider involvement

Question	Answer
4. Question for sexual abuse: Have you ever been emotionally, physically, or sexually victimized at any time during your life?	<input type="radio"/> Yes <input type="radio"/> Never
5. Question for physical abuse (by partner): Have you ever been afraid for your safety in your intimate relationships?	<input type="radio"/> Yes <input type="radio"/> Never
6. Question for pain severity: During the last four weeks, how much bodily pain have you had?	<input type="radio"/> Very severe <input type="radio"/> Severe <input type="radio"/> Moderate <input type="radio"/> Mild <input type="radio"/> None

GUIDELINES AND FLAGS FOR REFERRING TO A MENTAL HEALTH PROVIDER

Consider involvement

Involve quickly

Question	Answer	Scoring
7. Question for somatic symptoms and related anxiety: For the last six months or longer, have you worried about physical symptoms that you believe are serious?	<input type="radio"/> Yes <input type="radio"/> No	Question Origin If the response is "Yes," then the clinician should ask: "Is this currently causing you distress in your life?" and "Would you like to see someone to discuss this in more detail?" If the patient agrees that he/she is very distressed and would like to see someone, then the clinician should refer to a mental health professional (provided the patient agrees).
8. Question for impairment: During the last four weeks, how much does pain (or other symptoms) interfere with your normal activities (including work both outside the home and housework)?	<input type="radio"/> Extremely <input type="radio"/> Quite a bit <input type="radio"/> Moderately <input type="radio"/> A little bit <input type="radio"/> Not at all	Question Origin Patients answering "Quite a bit" or "Extremely" to this question (question 8 of SF-36) represent 26% of patients with functional gastrointestinal disorders whose physical component score is 2 standard deviations below the population norm. ^{1,2}
9. Question for drug/alcohol abuse: In the past year, how often have you used alcohol (for men, 5+ drinks/day, for women, 4+ drinks/day)/tobacco products/prescription drugs for nonmedical reasons/and/or illegal drugs?	<input type="radio"/> Daily or Almost Daily <input type="radio"/> Weekly <input type="radio"/> Monthly <input type="radio"/> Once or Twice <input type="radio"/> Never	Question Origin This sample question is taken from the National Institute for Drug Abuse Drug Screening Tool (http://www.drugabuse.gov/nmassist/). Rationale for Red Flag Scoring Patients who answer "Daily or Almost Daily" to any of these questions are likely to have a serious drug or alcohol addiction. The clinician should assess further and determine if a referral to specialty treatment is warranted.

Hospital Anxiety and Depression Scale (HADS)

(Zigmond and Snaith, 1983)

The items on the questionnaire that relate to **anxiety** are

- I feel tense or wound up
- I get a sort of frightened feeling as if something bad is about to happen
- Worrying thoughts go through my mind
- I can sit at ease and feel relaxed
- I get a sort of frightened feeling
- I feel restless and have to move about
- I get sudden feelings of panic

Each item: 0-3; Cut off: 8/21

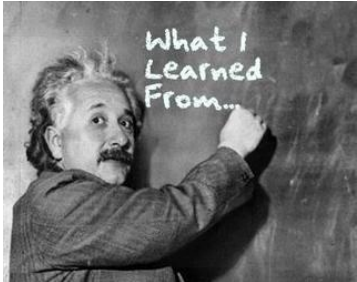
Anxiety (HADS-A): -specificity: 0.78
-sensitivity: 0.9.

The items that relate to

- I still enjoy the things I used to enjoy
- I can laugh and see the funny side of things
- I feel cheerful
- I feel as if I am slowed down
- I have lost interest in my appearance
- I look forward with enjoyment to things
- I can enjoy a good book or radio or TV programme

Depression (HADS-D): -specificity: 0.79
-sensitivity of 0.83.

(Bjelland et al 2002)



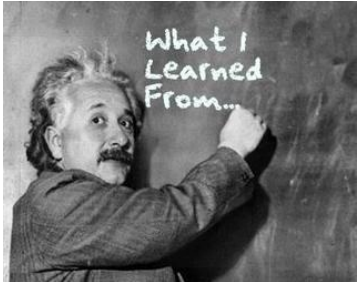
Take Home Messages (I)

Interplay is still a **complex matter** (chicken or egg?)

PSY comorbidities should be systematically **checked** and **treated** in FGID patients

PSY therapies (TCA/SSRI, cognitive behavioural therapy, gut-directed hypnotherapy, etc.) can be **effective** interventions in **FGID symptoms**

In FGID patients with high psychological burden, **early PSY interventions** may alter disease course and break the vicious cycle of **unnecessary investigations, interventions, and excess healthcare utilisation**.

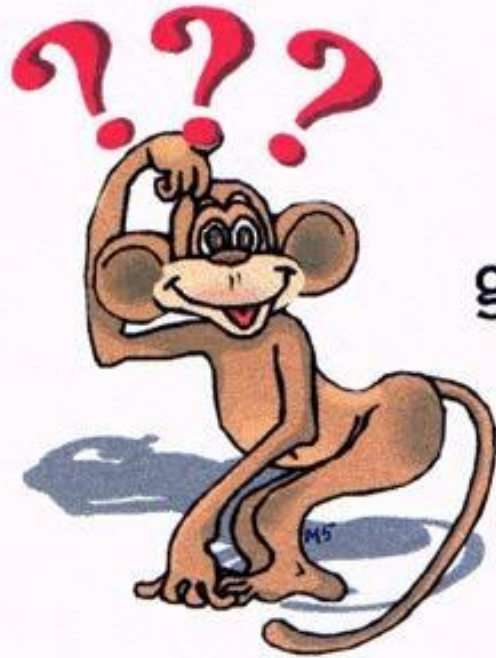


Take Home Messages (II)

Psychiatrist/psychologist employment is still hindered by a **lack of trained therapists and available services**.

Treatment of FGID symptoms in the patients with anxiety and depression can **improve their PSY** symptoms.

A **multidisciplinary** management of FGID patients (mainly in tertiary care) is mandatory



Questions
are
guaranteed in
life;
Answers
aren't.

