FUNCTIONAL GASTROINTESTINAL DISORDERS AND PSYCHIATRY

Holly S. Peek, M.D./MPH

Associate Medical Director, Klarman Eating Disorders Center, McLean Hospital

Instructor in Psychiatry, Harvard Medical School

OVERVIEW

- Case
- Defining Functional Gastrointestinal Disorders (FGIDs)
- Impact of FGIDs
- Historical Perspective
- Biopsychosocial Model of FGIDs
  - Brain-Gut Axis
- Treatment

CASE

- 14 year old female, no past psychiatric history, referred to mental health clinic.
- Viral GI illness at the beginning of her 9th grade school year with diarrhea and vomiting resulting in missing a week of school. Acute illness has now resolved.
- Since then, she has reported a diffuse abdominal pain associated with frequent diarrhea and nausea on most days.
- Has started missing school or spending much of the day at school nurse.

CASE

- Medical workup by pediatric gastroenterologist is negative, no apparent medical cause for these persistent symptoms.
- Has been diagnosed with FGID: irritable bowel syndrome (IBS-D) and functional nausea.
- Treated with anti nausea and IBS-D meds. Symptoms persist.

CASE

- GI requests psychiatric consultation to evaluate psychological factors affecting current clinical picture.
- Patient and parents are confused that they were referred to a psychiatrist for these GI symptoms.
- “They think this is all in my head!”
- Patient associates current anxiety to her GI symptoms. She reports being anxious to go to school because worried will have diarrhea or vomit at school, distracted by her pain most of the day.
- What do you do?

“I find this hard to swallow”

“I feel butterflies in my stomach”

“I cannot stomach this any longer”

DEFINING FUNCTIONAL GI DISORDERS

FUNCTIONAL GI DISORDERS DEFINITION

- Disorders of the gut-brain interaction
- Classified by GI symptoms related to:
  - **Motility disturbance-** movement of food and waste through GI tract
  - **Visceral hypersensitivity-** heightened experience of pain in internal organs
  - **Altered mucosal and immune function-** changes in the gut's immune defenses
  - **Altered gut microbiota-** changes in the community of bacteria in the gut
  - **Altered CNS processing-** changes in how the brain sends and receives messages from the gut

ROME IV CLASSIFICATION

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

ROME IV CLASSIFICATION

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
F2. Functional anorectal pain
- F2a. Levator ani syndrome
- F2b. Unspecified functional anorectal pain
- F2c. Proctalgia fugax

F3. Functional defecation disorders
- F3a. Inadequate defecatory propulsion
- F3b. Dyssynergic defecation

G. Childhood Functional GI Disorders: Neonate/Toddler

G1. Infant regurgitation
G2. Rumination syndrome
G3. Cyclic vomiting syndrome (CVS)
G4. Infant colic
G5. Functional diarrhea
G6. Infant dyschezia
G7. Functional constipation

H. Childhood Functional GI Disorders: Child/Adolescent

H1. Functional nausea and vomiting disorders
- H1a. Cyclic vomiting syndrome (CVS)
- H1b. Functional nausea and functional vomiting
  - H1b1. Functional nausea
  - H1b2. Functional vomiting
- H1c. Rumination syndrome
- H1d. Aerophagia

H2. Functional abdominal pain disorders
- H2a. Functional dyspepsia
  - H2a1. Postprandial distress syndrome
  - H2a2. Epigastric pain syndrome
- H2b. Irritable bowel syndrome (IBS)
- H2c. Abdominal migraine
- H2d. Functional abdominal pain – NOS

H3. Functional defecation disorders
- H3a. Functional constipation
- H3b. Nonretentive fecal incontinence

ROME IV CLASSIFICATION

IRRITABLE BOWEL SYNDROME

- Abdominal pain at least 4 days per month associated with one of more of the following:
  - Related to defecation
  - A change in frequency of stool
  - A change in form (appearance) of stool
  - After appropriate evaluation, the symptoms cannot be fully explained by another medical condition

FUNCTIONAL NAUSEA

- Must include all of the following for the last 2 months:
  - Bothersome nausea as the predominant symptom, occurring at least twice per week, not related to meals
  - Not consistently associated with vomiting
  - After appropriate evaluation, the nausea cannot be fully explained by another medical condition

IMPACT OF FUNCTIONAL GI DISORDERS

EPIDEMIOLOGY

- FGIDs are the most common consultations to pediatric gastroenterology.
- U.S. based study; prevalence in a survey of mothers of children 0-18:
  - Infants/Toddlers 24.7%
  - Children/Adolescents (4-18) 25%
  - Prevalence of FGIDs was significantly higher in children whose mothers also met criteria for FGID.
- Latin American based study; prevalence in a survey of mothers of children 4-18: 21.2%

EPIDEMIOLOGY

- Lower QoL compared to those without FGIDs
  - Increased psychological distress
  - Increased doctor and hospital visits
  - Increased absenteeism (school, parental work, and day care)
  - Poor physical and social functioning
- 1/3 of children with FGIDs will continue to have these issues into adulthood, despite treatment.
- Adults with recurrent abdominal pain as children:
  - Greater use of psych meds
  - Greater susceptibility to physical illness
  - Higher rates of anxiety and depressive symptoms

HEALTHCARE COSTS

- Costly condition in terms of:
  - Loss of time from work
  - Medication use
  - Repeated physician visits and hospitalizations
  - Multiple medical investigations
  - Generally poor treatment outcome
- Adult patients with IBS use 50% more healthcare resources than those without IBS.
  - $20 billion per year in direct and indirect costs

HEALTHCARE COSTS

- Higher pediatric annual mean total cost/person:
  - $1099 healthy controls
  - $3440 chronic constipation
  - $6104 chronic abdominal pain (consultations and investigational tests)
- From 1997-2009: annual mean cost of pediatric FGID inpatient admissions increased from $6115 to $18,058, despite length of stay remaining the same.

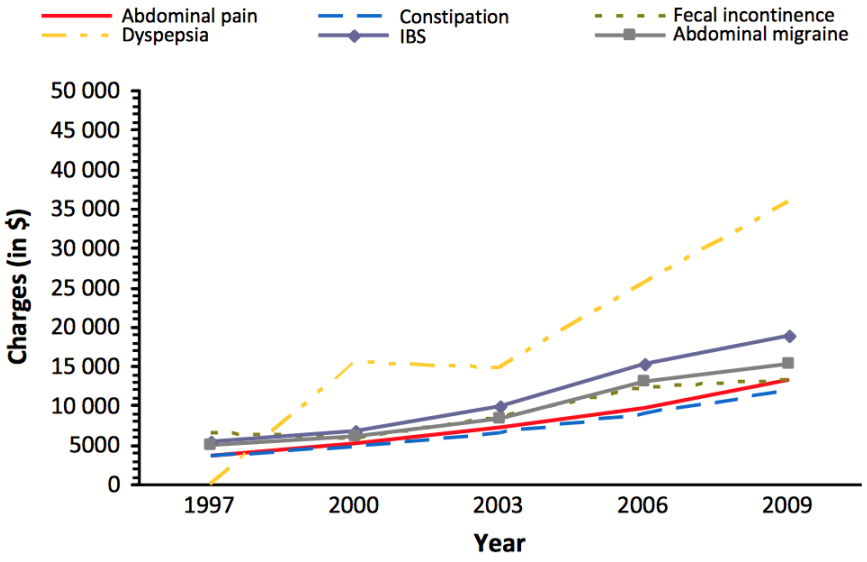


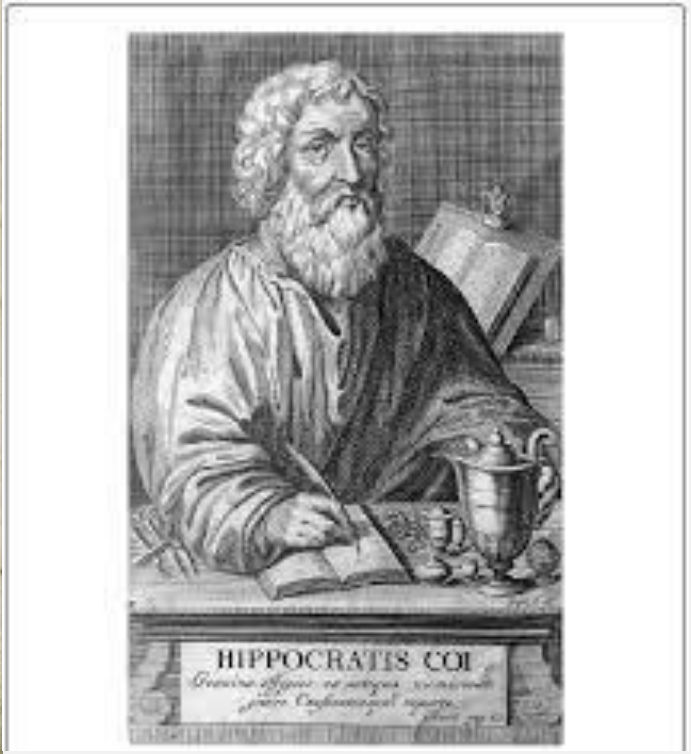
Figure 3 The total mean charge per discharge with a principal diagnosis of an FGID from 1997 to 2009.

HISTORICAL PERSPECTIVE

HISTORICAL PERSPECTIVE

HOLISM

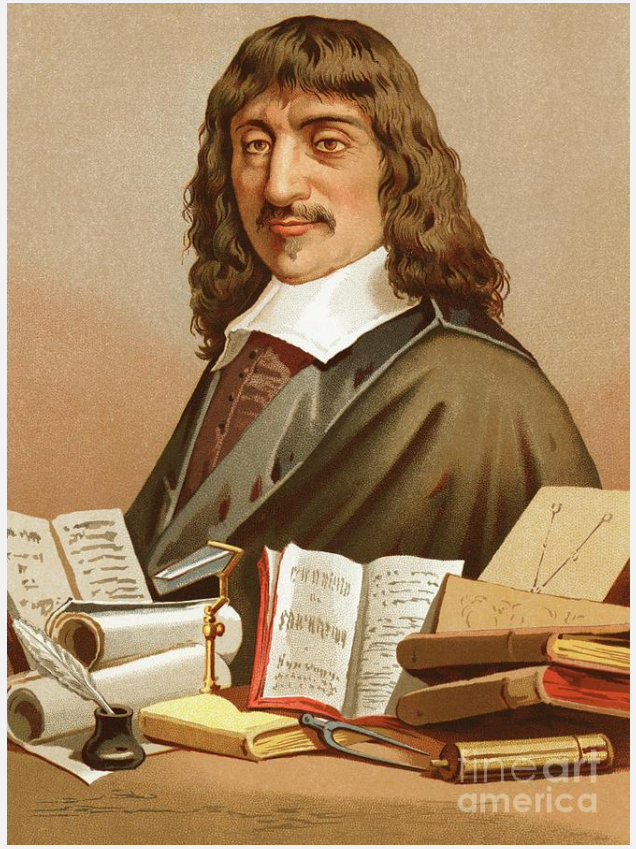
- Mind and body are integrated and inseparable.
- Takes into account the whole person rather than only the diseased part.
- Passions and emotions could lead to the developmental of medical disease.



HISTORICAL PERSPECTIVE

DUALISM

- Descartes, 1637: Separation of the thinking mind from the machine-like body.
- Human dissection became permitted.
- Understanding of disease through pathology.
- Centuries of developments of new diagnoses and treatment.

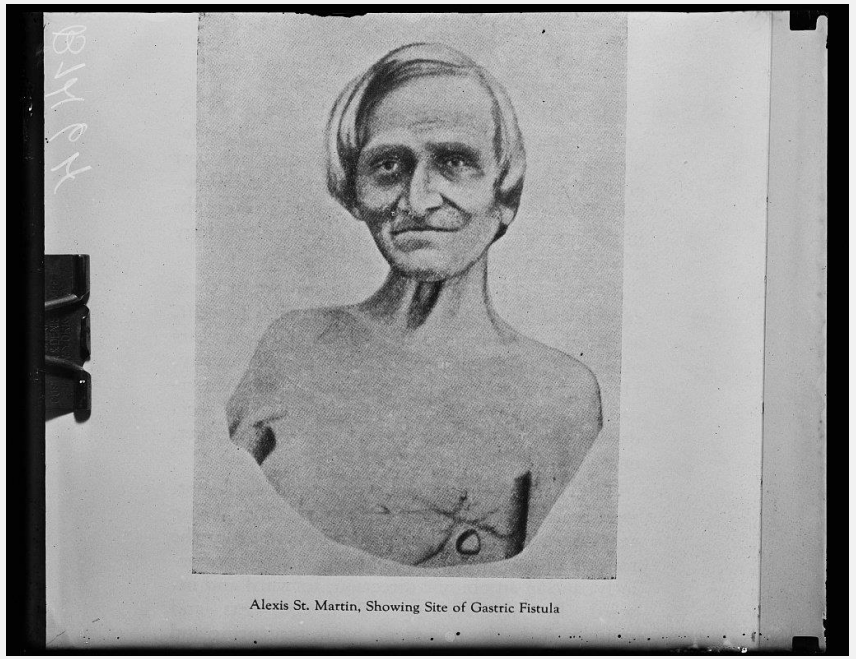


HISTORICAL PERSPECTIVE

- Mind-Body Dualism
  - Less understanding of symptoms or behaviors in absence of pathology.
- Mental illness or physical symptoms in absence of pathology were considered to be less legitimate than structural disease.

HISTORICAL PERSPECTIVE

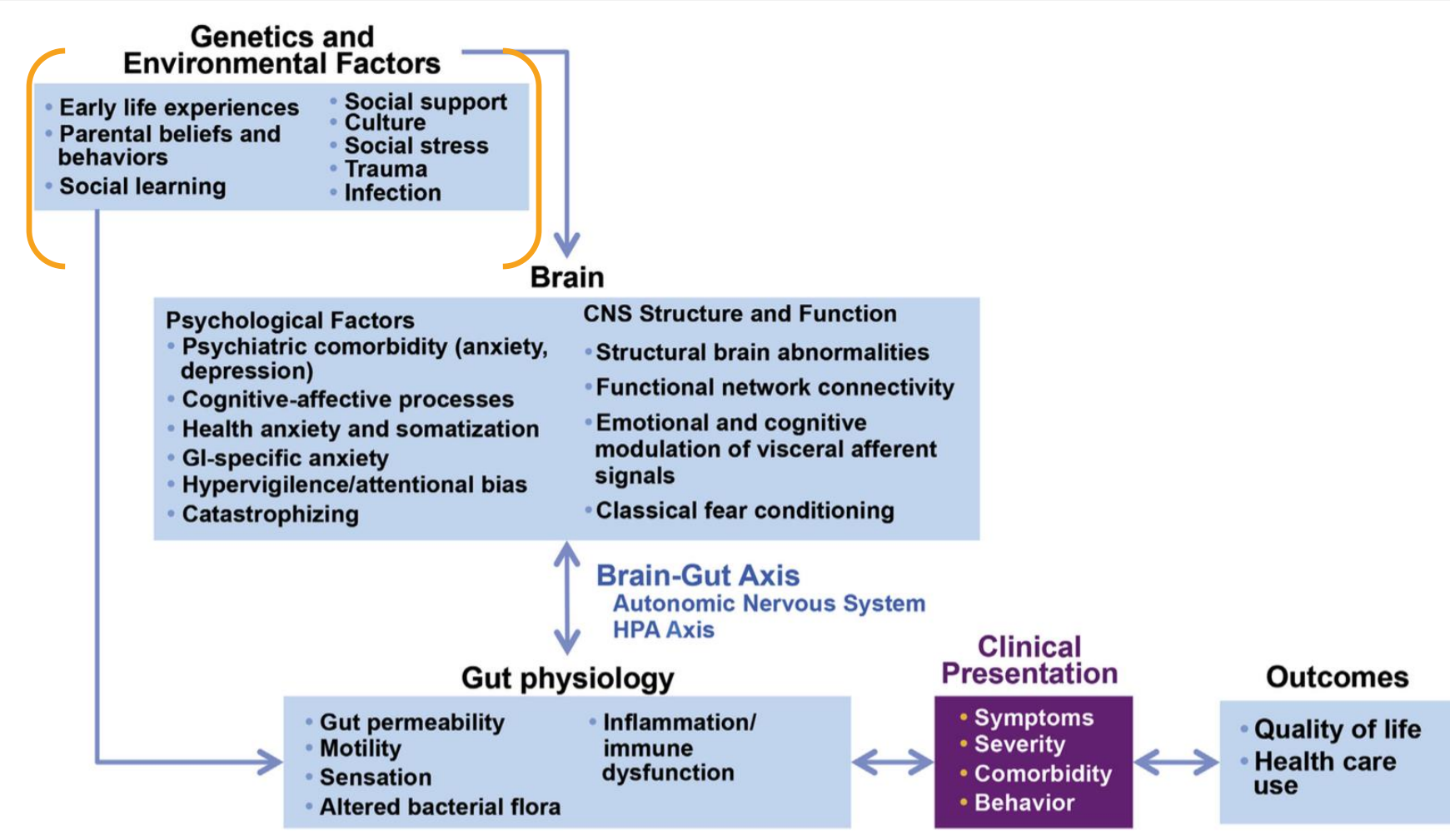
- Early observations and experiments of Brain-Gut Behavior:
  - 1800s William Beaumont: association of anger and fear with gastric mucosal morphology and function.
  - 1900-1959
    - Cannon: cessation in bowel activity among cats reacting to growling dog.
    - Wolf and Engel: different emotional states are associated with changes in gastric function.
    - Almy: experiments correlating mood/anxiety with motility.



HISTORICAL PERSPECTIVE

- 1960s-1980s
  - Technology developed to test gut functioning.
- Physiological studies did not appropriately explain symptoms of IBS.
  - Poor correlation between altered motility and painful symptoms.
- Psychological reports showed that patients with IBS had high frequency of psychological distress.
- Difficult to develop a unifying concept of IBS and other gut disorders that didn't have organic/pathological evidence of disease.

BIOPSYCHOSOCIAL MODEL OF FUNCTIONAL GI DISORDERS


Genetics and Environmental Factors
Early life experiences
Parental beliefs and behaviors
Social learning
Social support
Culture
Social stress
Trauma
Infection
Brain
Psychological Factors
Psychiatric comorbidity (anxiety, depression)
Cognitive-affective processes
Health anxiety and somatization
GI-specific anxiety
Hypervigilence/attentional bias
Catastrophizing
CNS Structure and Function
Structural brain abnormalities
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Emotional and cognitive modulation of visceral afferent signals
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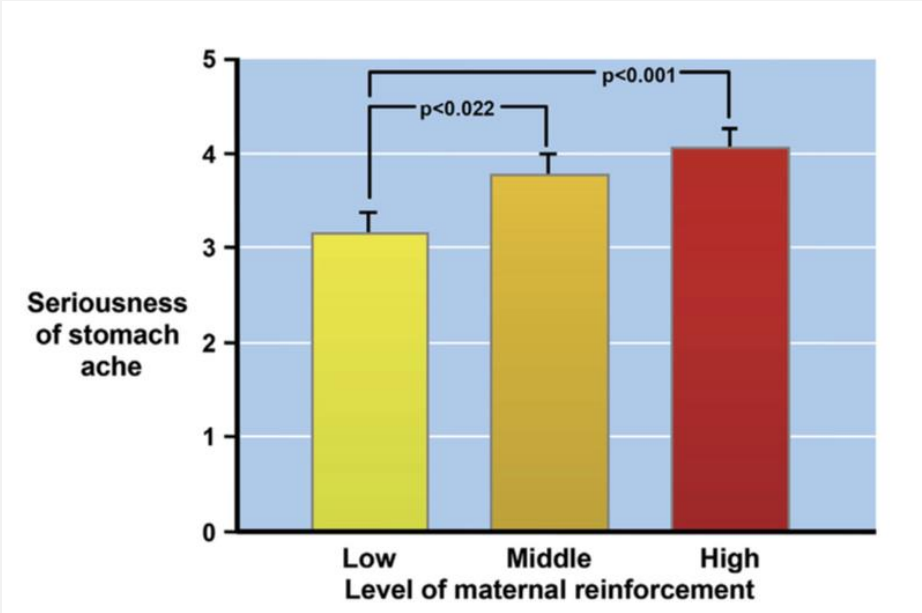
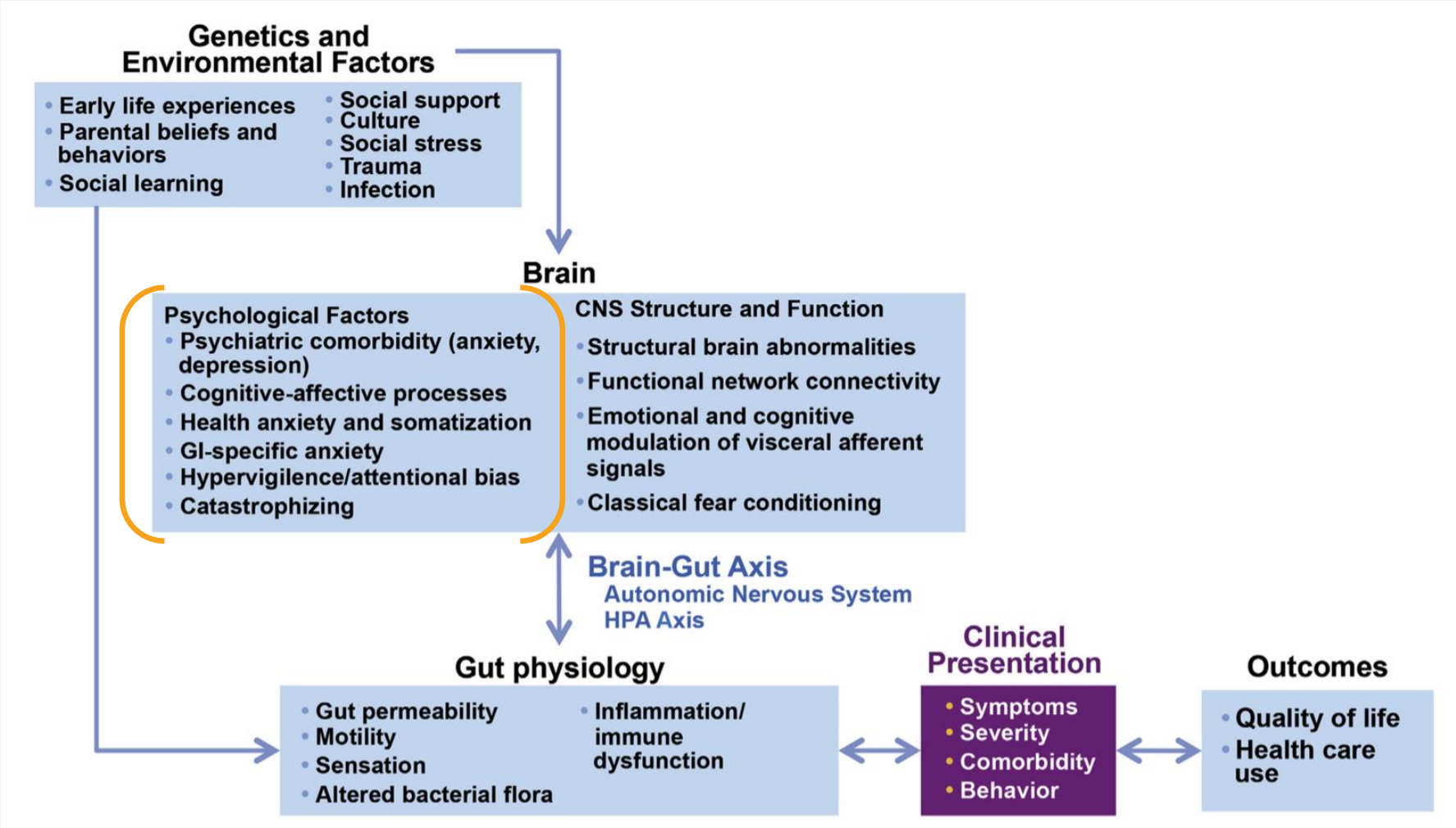
Altered bacterial flora
Inflammation/ immune dysfunction
Clinical Presentation
Symptoms
Severity
Comorbidity
Behavior
Outcomes
Quality of life
Health care use

BIOPSYCHOSOCIAL MODEL

- **Environmental Influences**
  - Familial patterns of FGID
    - Parental beliefs and behaviors
  - Positive reinforcement and reward
  - Parental psychological status
- **Adverse Life Events**
  - Physical punishment, emotional abuse, and sexual abuse
  - Chronic life stress is the main predictor of IBS symptom intensity
  - Stress can affect treatment outcomes

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BIOPSYCHOSOCIAL MODEL

- Psychological Distress
  - Predictor of IBS
  - Also occurs as a consequence of bodily symptoms and related quality of life impairment
  - Depression co-morbidity is approx. 30%
    - SI is present between 15-38% of patients with IBS
    - Linked to poor outcomes, high cost utilization, poor QoL, functional impairment, poor treatment engagement and outcomes
  - Anxiety disorder co-morbidity 30%-50%
    - Heightened autonomic arousal
    - Interferes with GI sensitivity and motor function

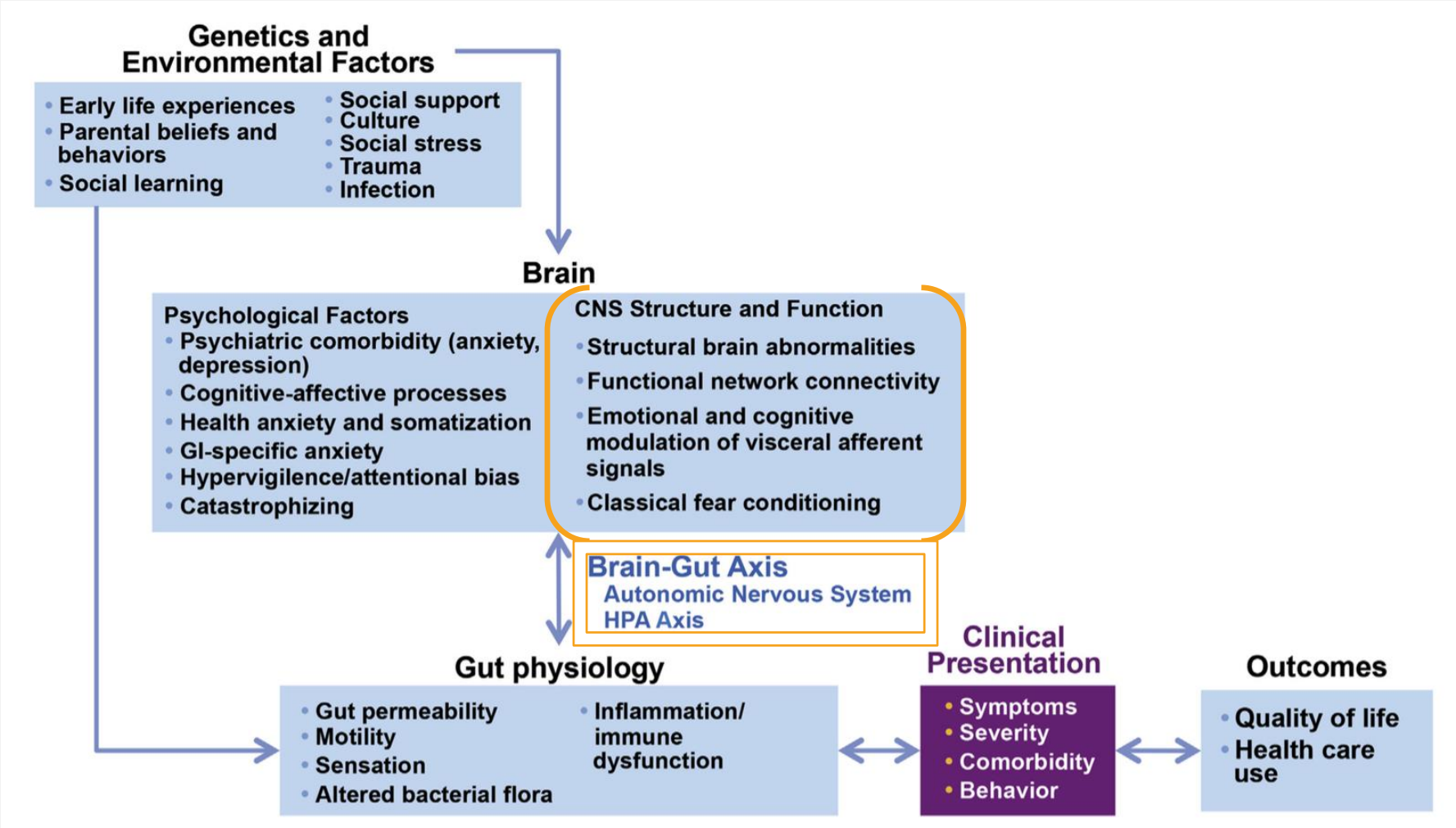
BIOPSYCHOSOCIAL MODEL

DSM V SOMATIC SYMPTOM DISORDER

- May or may not be medically explained
- Distressing and disabling
- Associated with excessive and disproportionate thoughts, feelings, and behaviors for more than 6 months

DSM IV SOMATIZATION DISORDER

- Somatization
  - No medical cause
  - Response to psychosocial stress
  - Measured by quantifying number of unexplained symptoms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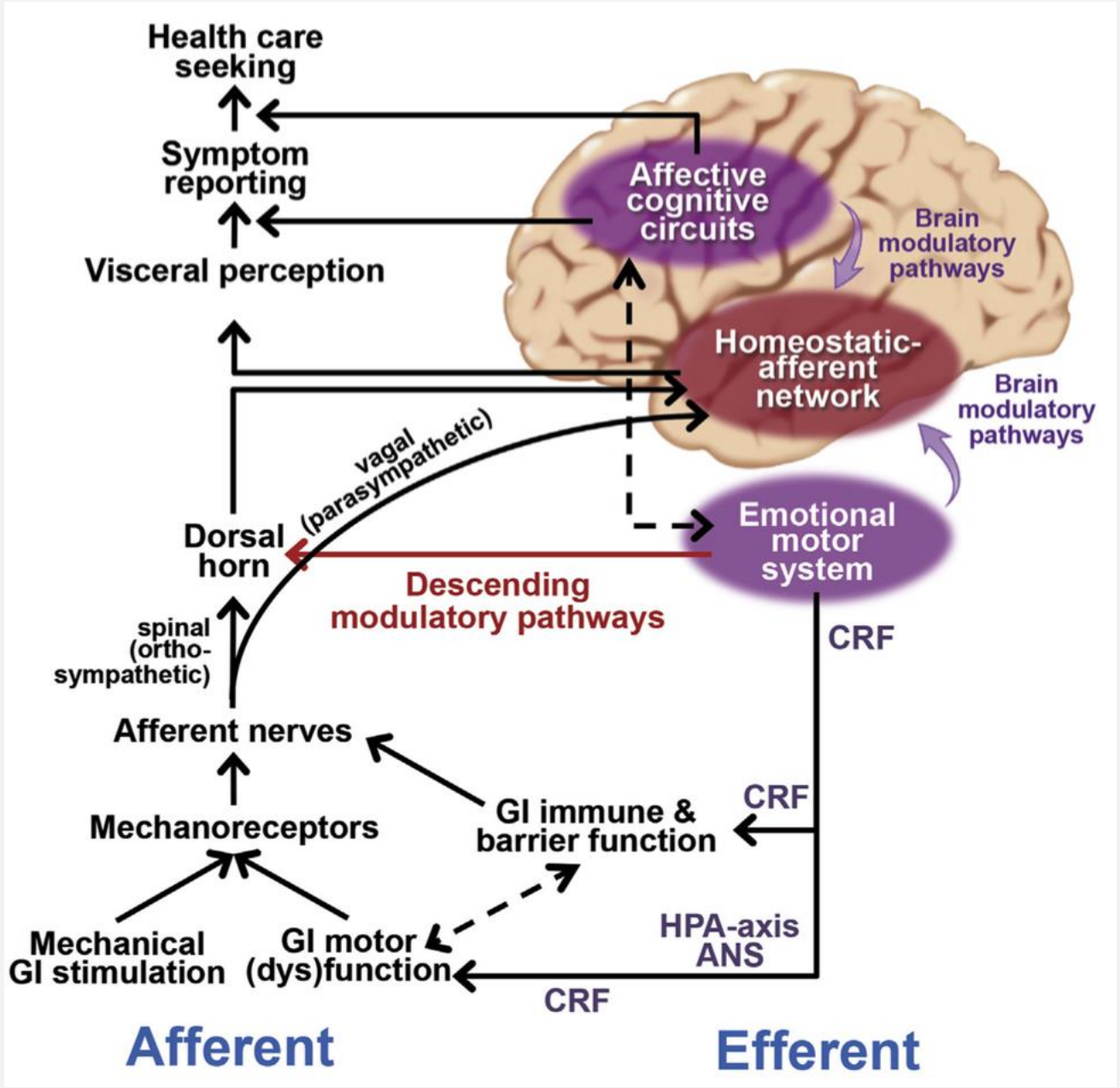
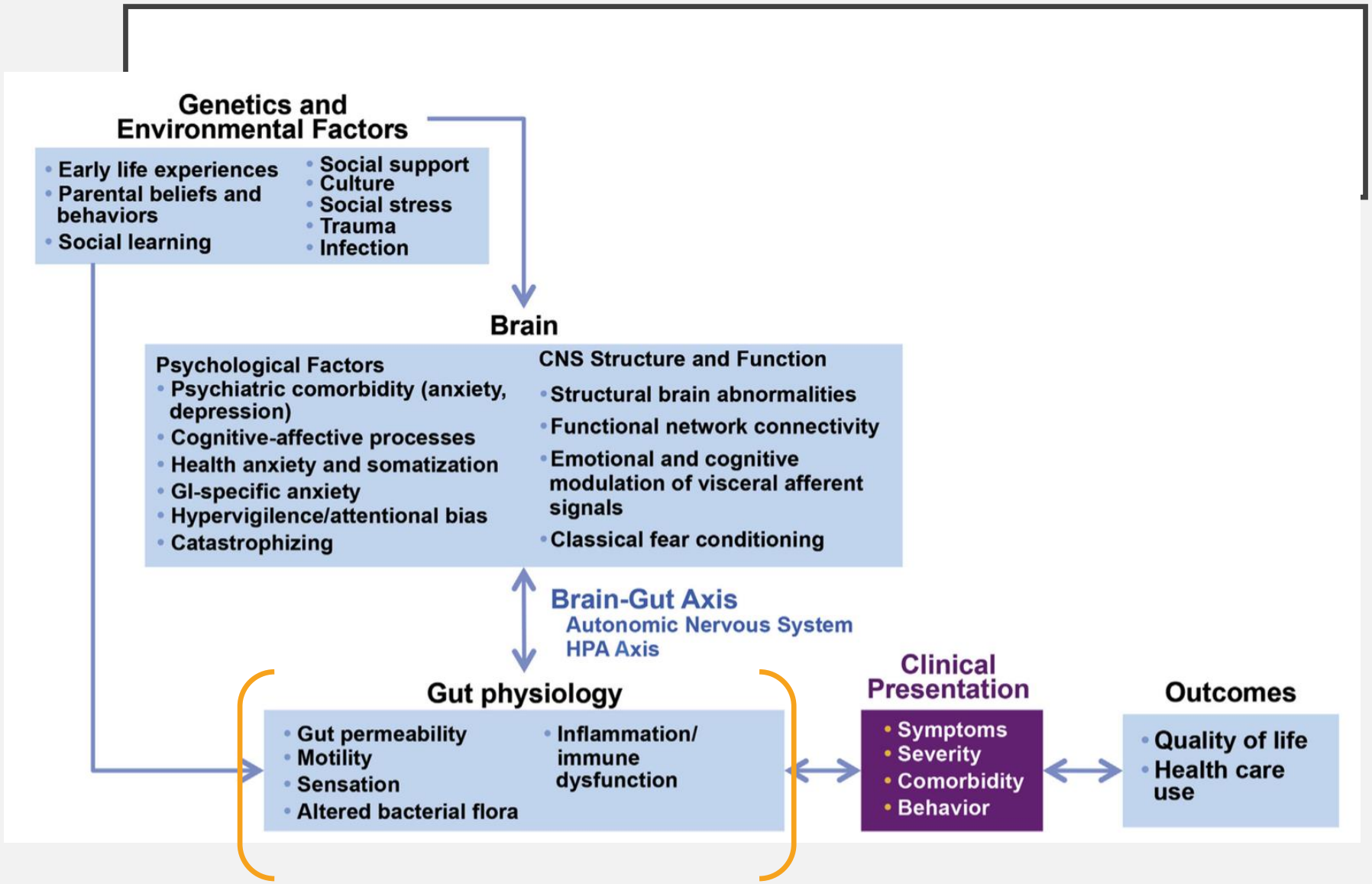
Brain-Gut Axis

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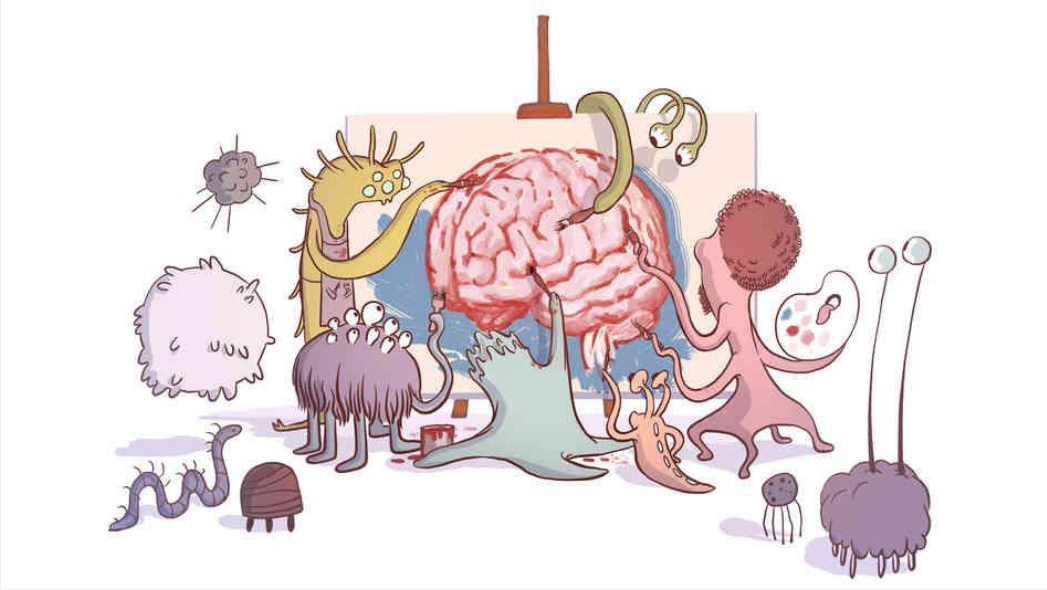
BIOPSYCHOSOCIAL MODEL

- **Gastric Motility**
  - Stress induced reduction in gastric motility and emptying
  - Impairment in gastric accommodation during experimentally induced anxiety in healthy subjects
- **Colonic Motility**
  - IBS patients have exaggerated motility responses to physical and psychological stress
    - Exaggerated response to injection of CRF when compared to healthy subjects
  - Changes in stool frequency and consistency, abdominal distension
- **Colonic mucosa**
  - influence of stress on colonic permeability and low-grade mucosal and systemic inflammation

BIOPSYCHOSOCIAL MODEL

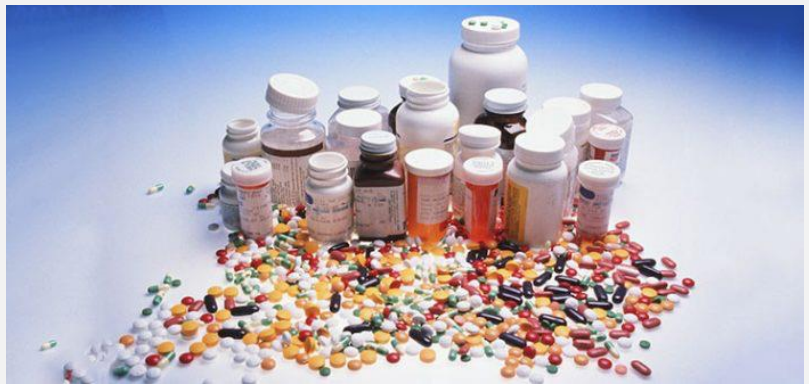
- Microbiome-Gut-Brain Axis
  - IBS symptoms have been associated with alterations in microbiota composition, probiotics have been shown some efficacy
    - Larger studies are needed



TREATMENT OF FUNCTIONAL GI DISORDERS

CENTRAL NEUROMODULATORS

- Peripherally acting agents will likely be 1st line for a GI physician.
- TCAs, SSRIs, SNRIs, atypical antipsychotics, and others are considered the central neuromodulators.
  - Considered when patients do not respond to peripherally acting agents
- Psychiatrist may be consulted in use of these medications.
- Not FDA approved for these conditions, but are generally accepted for the treatment of FGIDs.



TRICYCLICS

Amitriptyline

Desipramine

Imipramine

Nortriptyline

- 1st line for treating pain related FGIDs
  - Pain helped mostly by inhibition of NET
- Helpful in reducing diarrhea because anticholinergic effects
- Sedating and helpful for sleep

SSRIS

Citalopram
Escitalopram
Fluoxetine
Paroxetine
Sertraline

- Primarily inhibits SERT
- Provides benefit when anxiety and depression related symptoms are dominant
- SSRIs more likely to cause diarrhea, helpful with constipation prominent symptoms (IBS-C)
- Not as helpful for pain
- If pain also present, can be used with TCA or choose SNRI

SNRIS

Duloxetine

Venlafaxine

- Lower side effect burden than TCAs with similar pain reduction
- Less constipating than TCAs and more pain relief than SSRIs
- Diabetic neuropathy, fibromyalgia, chronic musculoskeletal pain
  - Not as studied for visceral pain, but commonly used similarly

ATYPICAL ANTIPSYCHOTICS

Aripiprazole
Brexipiprazole
Olanzapine
Quetiapine

- Second line agents for various FGIDs
- Used to augment the pain benefit for TCAs or SNRIs (inhibits NET)
- Useful in treatment of nausea Zyprexa and Seroquel
- Benefit of also reducing symptom related anxiety and insomnia

MISCELLANEOUS AGENTS

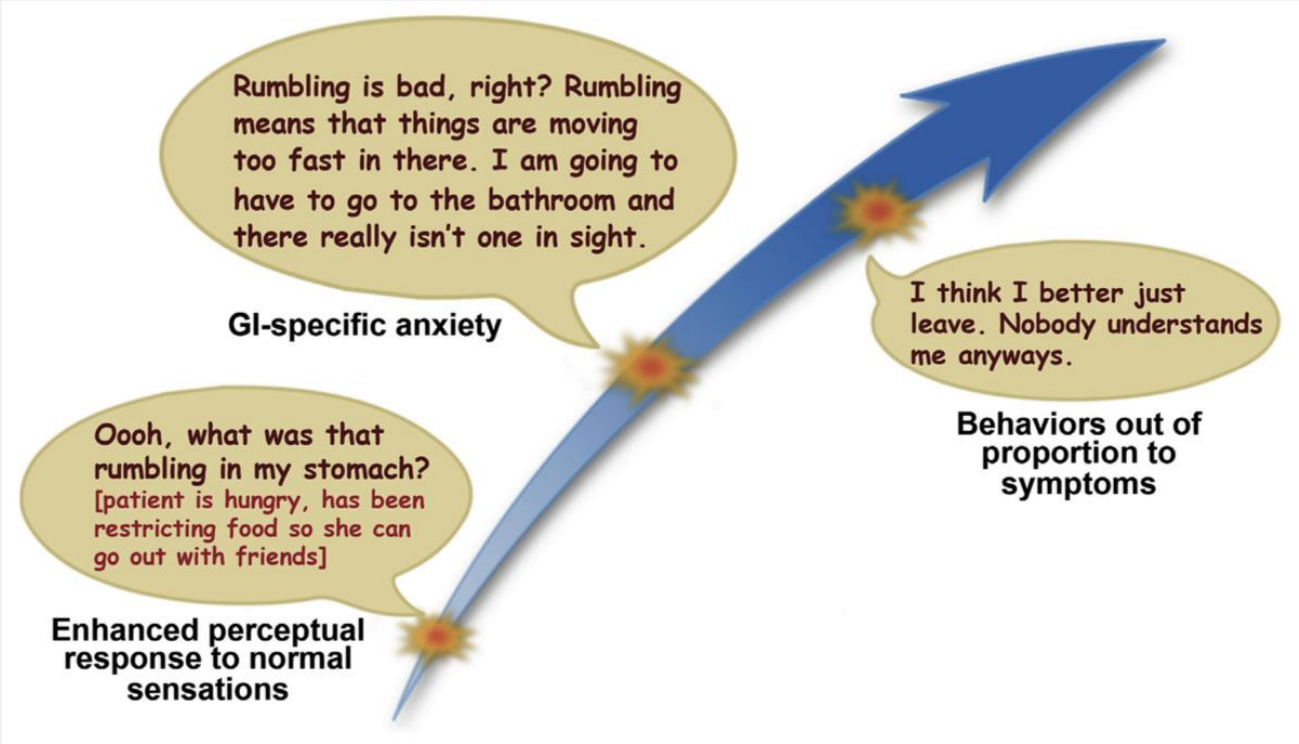
Buspirone

Mirtazapine

- Buspirone: 5HT1A agonist
  - helpful for enhancing gastric relaxation in patients with functional dyspepsia and post-prandial distress; anxiety
- Mirtazapine: selective Alpha-2 agonist, also blocking 5HT2, 5HT3, and H1
  - treating chronic nausea, dyspepsia, weight loss, insomnia

COGNITIVE BEHAVIORAL THERAPY

- Psychoeducation
- Relaxation strategies
- Cognitive restructuring
- Problem solving skills
- Exposure techniques



GUT-DIRECTED HYPNOTHERAPY

- Generally shown to be effective, may affect:
  - Visceral sensitivity
  - GI motor function
  - Psychological distress
- Based on muscular and mental relaxation.
- Hypnotic suggestions are used to focus on the symptoms or to distract from them.
- Goal is to develop ability to feel patient is able to control the symptoms.
  - Suggestions of normalizing GI function, such as "a river flowing smoothly or a blocked river cleared by the patient"

CONCLUSION

CASE CONCLUSION

- 14 yo female dx with IBS-D and functional nausea. Peripherally acting agents prescribed by GI minimally helpful.
- Patient has developed a generalized anxiety/avoidance symptoms, also has diarrhea, pain, and nausea.
- Treatment Plan:
  - Psychoeducation: explain to patient and family the concept of Gut-Brain Axis.
  - Validate symptoms and the need to try treating symptoms using centrally acting agents.
  - Rx: Cymbalta (SNRI) chosen for impact on GAD and pain; Amitriptyline chosen for impact on diarrhea, pain.
  - Refer to CBT therapist and/or Gut-Directed Hypnotherapy.

CONCLUSION

- FGIDs are disorders of Brain-Gut interaction.
- FGIDs impact a significant number of people, significantly impact quality of life, and are associated with increasing healthcare costs.
- FGIDs have a high psychiatric co-morbidity, including anxiety, depression, and suicidality.
- FGIDs are best explained by using the Biopsychosocial Model.
- Many psychiatric medications can help treat FGID symptoms and psychiatric co-morbidities.
- Behavioral and psychological approaches are also helpful treatments.

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