The Spectrum of Functional GI Disorders

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Introduction

Functional Gastrointestinal Disorders (FGID), also known as Disorders of Gut-Brain Interaction (DGBI), can manifest with a wide variety of symptoms caused by abnormalities within gastrointestinal motility, visceral hypersensitivity, altered mucosal and immune function, altered gut microbiota, and central nervous system gut afferent input processing. Gut dysfunction has been closely linked to emotional wellbeing and life stressors. Traditional Buddhist thinkers and Ancient Greeks Plato, Aristotle, and Hippocrates first postulated the concept that the mind and body function as singularity, referred to as holism from the Greek work *holos* or whole. In the fourth century, a paradigm shift occurred which shifted from holism to biomedicine. In 1637, Rene Descartes proposed the separation from mind and body known as dualism; this concept has dramatically affected the way we evaluate patients in modern medicine [1]. Ignorance about the biopsychosocial model of health can lead to dismissing illness without pathology as trivial or behavioral and some physicians find it difficult to empathize with their patients [2]. The concept of holism started to remerge in the nineteenth century. In 1833, William Beaumont demonstrated the association of emotions such as anger and fear with gastric mucosal morphology and function [3]. There was a surge of studies reporting the effects of emotion on gastrointestinal function (motility and sensory) in the twentieth century. These data provided evidence that the gut is physiologically responsive to external stimulation and subsequent emotional responses.

Introduction of the biopsychosocial model in the late 1970s set the stage for further research and understanding of FGID. In 1977, George Engel, an internist and psychoanalyst, challenged the tradition biomedical approach which looked at disease to be "fully accounted for by deviations from the normal of measurable biological variables" and proposed a new holistic theory that illness results in the combination of biological, psychological, and social components interacting at variable degrees [3–5]. The combination of these components determines disease severity (Fig. 19.1) [6]. This biopsychosocial model allowed better understanding of human illness by integrating biomedical thought and clinical observations, provided a framework to evaluate biomedical processes and how they are affected by psychosocial factors leading to a unique patient experience, and lastly it created a multidisciplinary team approach to assessing GI conditions by including a biopsychosocial assessment. This changed research outcomes dramatically, no longer focusing solely on morbidity and mortality but rather health-related quality of life, health care use, daily function, and symptom severity.

The complex interaction between the brain, enteric nervous system, endocrine, and the immune system, which helps to regulate the bowel function, is called the brain gut or more recently the microbiome brain-gut axis [7]. The brain-gut axis is comprised of the enteric nervous system, which is broadly organized into the myenteric and submucosal plexuses and communicates with the brain through the neural pathways, as well as the immune and endocrine systems [8]. The sympathetic and parasympathetic branches of the autonomic nervous system (ANS) connect emotional arousal and central autonomic brain circuits with the enteric nervous system. This extensive neural network innervates visceral smooth muscles and other end-organs within the GI tract and regulates the GI secretory, sensory, motor, endocrine, and immune functions. This complex network communicates information from the emotional and cognitive centers of the brain via neurotransmitters to the gastrointestinal tract and vice versa [9]. However, the bowel function can be modulated by intrinsic neural circuits within the wall of the gastrointestinal tract bypassing the central nervous system via the myenteric and

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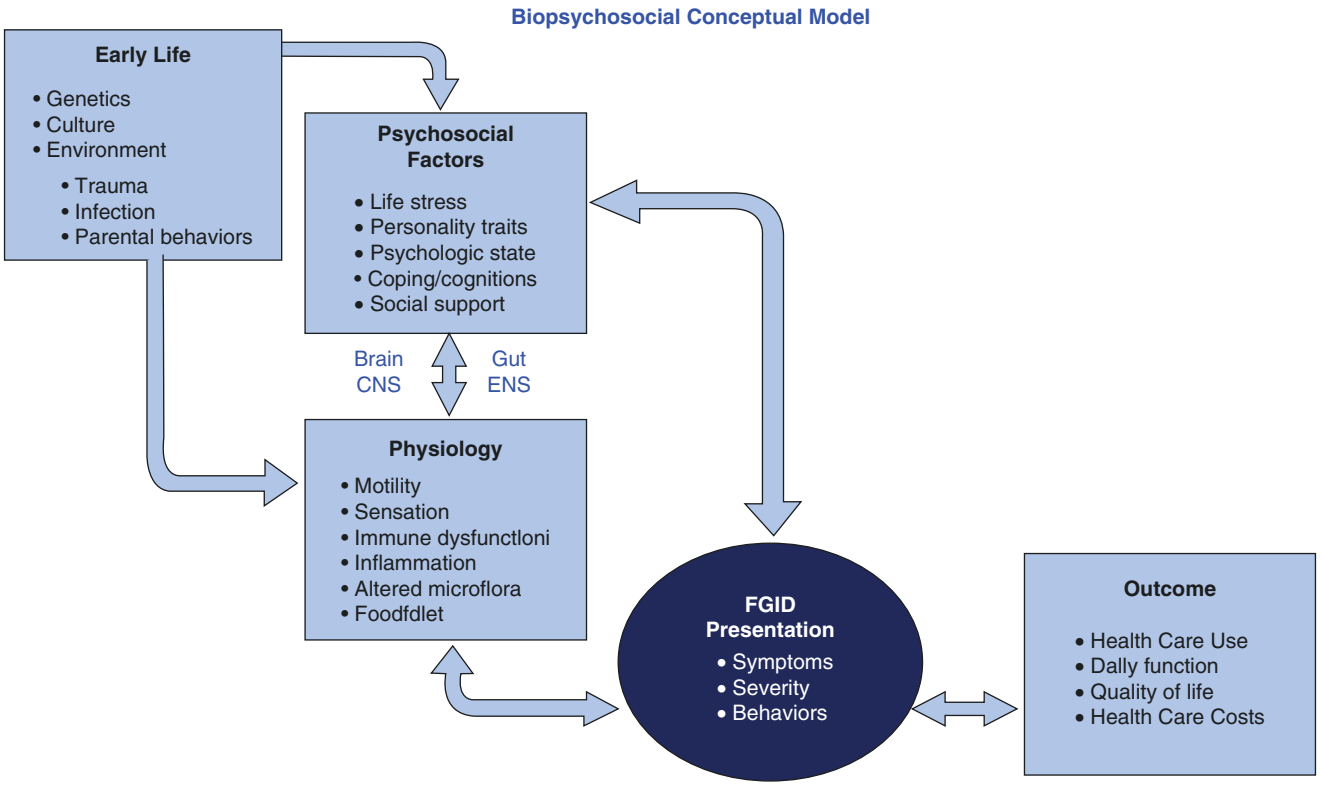

Fig. 19.1 A biopsychosocial conceptualization of pathogenesis, clinical experience, and effects of functional GI disorders. There is a relationship between early life factors (genetics, culture, and environment) that can influence the psychosocial milieu of the individual, their physiological functioning, as well as their mutual interaction (brain-gut axis). These factors influence the severity of the clinical presentation of the disorder and the clinical outcome. (Reproduced from Drossman et al. 1998 with permission from the Rome Foundation) [3]

submucosal plexuses of the enteric nervous system and other reflex circuits such as the gastrocolic and ileocolic reflexes. Gut luminal contents including the microbiome and immune system participate in this autoregulation. This complex neural network in conjunction with endocrine and immune system maintains gut and body homeostasis to ensure optimal bowel function for digestion and absorption of nutrients and elimination of waste. Symptoms can result from the disruption of gut function and homeostasis triggered by food (lactose and food intolerance), changes in gut microbiome-immune interaction (postinfectious IBS), or autonomic nervous system disease (diabetic gastroparesis) [7].

Disorders of the autonomic nervous system, such as postural orthostatic tachycardia syndrome (POTS) and diabetic neuropathy, can also manifest with gastrointestinal symptoms. These disorders are commonly associated with a broad spectrum of symptoms, for example, headaches, nausea, vomiting, and pain [10–12]. In addition to the gastrointestinal tract, the ANS also regulates cardiac function and the heart rate variability has been proposed as one of the objective measures of balance between the parasympathetic-sympathetic arms of the ANS. Gastrointestinal symptoms of autonomic dysfunction can be reproduced in the upright position with resolution of symptoms once the child is supine [13]. Frequently, patients with POTS or orthostatic intolerance may have overlapping gastrointestinal symptoms not produced by an orthostatic challenge. Orthostatic disorders are commonly associated with other comorbid conditions such as migraine headaches, fibromyalgia, chronic fatigue, nausea, sleep disorders, and abdominal pain [10]. It is important to differentiate symptoms that present with change in position versus those that are present irrespective of body position, as this will determine the treatment of choice.

Biopsychosocial Model of Functional Gastrointestinal Disorders

The main focus of the biopsychosocial model is the concept that illness is not a result of a single factor but rather a combination of factors involving early life (genetics, culture, and environment), psychosocial factors, and physiology which later impacts the interactions of the brain-gut (central nervous system-enteric nervous system) axis [7, 14, 15]. It is important that each aspect of the biopsychosocial model is addressed and treated. For example, if a patient presents with pain associated with IBS but also has depression and anxiety and a history of abuse, each of these areas can potentially

lead to the perception of pain and the patient's overall experience of illness [16]. The severity of symptoms affects the clinical outcome and vice versa. It is important to identify the severity of symptoms and limitations in daily functioning in order to determine an appropriate treatment plan. Equally important is the response from the family to the child's complaints, which may amplify the patient's symptoms and illness experience [17, 18]. When a physician validates patient's symptoms, engages them in conversation, and provides empathy, it not only builds trust but also reduces symptom severity and health care seeking behavior [19]. In the biomedical approach, both physicians and patients were in search of an organic disease as a cause for illness leading to increased health care costs due to referrals, tests, medications, and possible surgeries. This can lead to increased anxiety, frustration, and dissatisfaction among both the physician and patient. Breaking this cycle and approaching patients with DGBI by a biopsychosocial model is imperative to improving their quality of life and health care outcomes.

Genetic susceptibility influences future behaviors and experience of illness. DGBI can result from polymorphisms affecting the motor function, membrane permeability, and visceral sensitivity, which has been reported in patients with IBS [20, 21]. In addition, stress may affect epigenetic expression of these genes leading to visceral hypersensitivity and other motor function abnormalities in DGBI [22].

Culture plays an important role in the child's expectation and perception of their illness. Fitting in with the cultural and society norms and functioning as a meaningful contributor to society is critical to psychological wellbeing of an individual. Based on cultural norms and influences, this determines whether a patient seeks medical attention, is self-treated, or ignored. For example, in Mexico diarrhea is often not seen as an illness requiring medical attention since it is so common [23]. In Arapesh, pregnant women did not report morning sickness because they did not believe the child existed until after birth [24]. Even expression of pain varies among cultures [25]. The role of a physician is also very important within cultures, where some cultures accept patient-centered care as a norm with shared decision-making, where other cultures see this as a sign of weakness or lack of knowledge on behalf of the physician [26]. It is critical to understand the patient's belief system and set of cultural norms in order to involve them in decision-making.

Early life events involving feeding and elimination are often the first experiences in a child's life of confrontation. According to the psychoanalytic theory, the child's early innate impulses to eat and defecate meet external confrontation and naturally, they are prone to resolution of these conflicts. With time, they will learn to comply or resist environmental control of these functions by refusing to eat, defecate, or acting out. The behaviors learned during this time frame are pivotal in the development of autonomy, learning right from wrong, and adopting socially acceptable behaviors such as bowel functioning. Functional defecation disorders, for example, infant dyschezia and learned feeding disorders can develop due to confrontation experienced during early life [27]. Other children will develop abnormal patterns of defecation out of defiance or control leading to fecal incontinence and pain as toddlers.

Unresolved stress due to traumatic life events or daily life stressors can impact the way an individual experiences their illness in various ways (1) producing psychophysiological effects on gastrointestinal motor and sensory functioning, (2) amplifying symptoms due to brain processing of afferent gut input such as hypervigilance, and (3) developing poor coping skills and health care seeking [28–30]. It is important to recognize chronic and daily life stressors when establishing a treatment plan, as these events can lead to poor outcomes and decreased quality of life. A history of physical or sexual abuse has been linked to symptom severity and outcomes. Inflexibility and inability to recover or adapt to adverse early life events are possible mechanisms for increased risk of DGBI [31]. In cases where individuals have developed maladaptive behaviors, behavioral intervention is needed to correct these behaviors and change the way individuals view their illness [29].

Parental beliefs and behaviors through a child's life can have a positive or negative impact on how a child experiences illness. A child of a mother who reinforces illness behavior will have more reported severe abdominal pain and school absences than a child whose mother does not reinforce this behavior [17]. In a recent clinical trial, children reported more pain when parents showed sympathetic response to their complaints, compared to parents who ignored the complaints [32]. In addition, children's abdominal pain has been shown to be associated with parental anxiety and depression [33]. A child learns how to cope with various situations in life based on modeling their parent's response to their own experiences, the same way that parent's personality traits may also influence illness experience. For example, a parent who excessively worries or catastrophizes may also reward a child's somatic complaints reinforcing this illness behavior.

A child's psychological status may influence gastrointestinal physiology, leading to the development of a DGBI and its symptomatic and behavioral expression influencing outcomes. Psychological factors can be divided into either longstanding, or trait, features such as personality or psychiatric disorders and short-term, or state, features such as psychological distress. Though a patient's symptoms of anxiety and depression may not meet the criteria based on current psychiatric classification systems, this does not discredit their potential impact on functional gastrointestinal symptoms. Comorbid depression has been linked to poor outcomes in patients with DGBI, including increased health

care utilization, decreased functioning, poor treatment compliance, and overall poor quality of life [29]. Anxiety leads to increased autonomic arousal, which can interfere with gastrointestinal motility and sensitivity leading to hypervigilance and decreased pain tolerance [34]. Recognizing these conditions and familiarizing oneself with psychological and psychopharmacologic interventions can affect the long-term outcome of patients with DGBI [35, 36].

Approach to Patients with Disorders of Gut-Brain Interaction

A careful consideration of the biopsychosocial model in approaching patients with DGBI is critical in patient satisfaction and outcomes. Effective communication is an essential part of developing a trusting patient-physician relationship. Overreliance on technology to the detriment of effective communication can be counterproductive. Focusing on the four main principles of effective communication (active listening, addressing the patients' agenda, providing empathy, and validation of patients' beliefs and concerns) aids in improving diagnosis and clinical decision-making by creating a trusting environment in which patients feel comfortable sharing both their clinical and psychosocial information [37, 38]. This creates a holistic view of the patients' symptoms, allowing a provider to see the full impact it has on their health care quality of life. Effective communication allows patients to collaborate in their treatment plan through shared decision-making, improving patient compliance, and motivating them to share the responsibility of their disease burden. Effective verbal and nonverbal communication can decrease overall time spent on making a positive diagnosis by forming a trusting relationship where the patient feels comfortable sharing personal information and participating in shared decision-making. It allows the patient to feel heard, sharing their expectations and goals for the encounter, allowing for improved outcomes for the patient by reducing symptom severity, emotional distress, improves satisfaction and coping, improves adherence to treatment and decreased overall health care costs. For the provider, effective communication skills training has been shown to decrease emotional exhaustion and burnout. The provider-patient relationship is the most commonly reported indicator for physician satisfaction [39]. The Rome Foundation has made efforts to improve education for medical trainees by offering free study guides to improve communication skills (https://romedross.video/2YphMDd) and for self-learning educational videos (https://romedross.video/2KPTYzC). Table 19.1 is a list of verbal and nonverbal methods that can be applied to improve patient-provider communication [37]. In order to

Table 19.1 Verbal and nonverbal behaviors affecting communication

Behavior	Facilitates	Inhibits
Nonverbal		
Clinical environment	Private, comfortable	Noisy, physical barriers
Eye contact	Frequent	Infrequent or constant
Listening	Active listening—questions relate to what the patient says	Distracted or preoccupied (e.g., typing)
Body posture	Direct, open, relaxed	Body turned, arms folded
Head nodding	Well time	Infrequent, excessive
Body proximity	Close enough to touch	Too close or too distant
Facial expression	Shows interest and understanding	Preoccupation, boredom, disapproval
Voice	Gentle tone	Harsh, rushed
Touching	Helpful if well timed and used to communicate empathy	Insincere in inappropriate or not properly timed
Synchrony (arms, legs)	Concordant	Discordant
Verbal		
Question forms	Open ended to generate hypothesis	Rigid or stereotyped
	Closed ended to test hypothesis	Multiple choice or leading questions ("You didn't… did you?"
	Use of patient's words	Use of unfamiliar words or jargon
	Facilitates patient discussion by "echoing" or affirmative gestures	Interruptions, undue control of conversation
	Uses summarizing statements	Not done
Question/Interview style	Nonjudgmental	Judgmental
	Follows the lead of patient's prior comments (patient centered)	Follows own preset agenda or style
	Use of narrative thread	Unorganized questioning
	Appropriate use of silence	Interruptions or too much silence
	Appropriate reassurance and encouragement	Premature or unwarranted reassurance or encouragement
	Communicated empathy	Not provided or not sincere
Recommendations	Elicits feedback and negotiates	No feedback, directly states views
Asks/provides medical information	As appropriate to the clinical issues	Too many biomedical questions and too detailed information

(continued)

Table 19.1 (continued)

Behavior	Facilitates	Inhibits
Asks/provides psychosocial information	Elicits in a sensitive and nonthreatening manner	Ignores psychosocial data or asks intrusive or probing questions
Humor	When appropriate and facilitative	None or inappropriate humor

Permission from the Rome Foundation [37]

Table 19.2 Rome IV Foundation 12-step approach to patients with DGBI

1. Improve patient satisfaction and engage the patient in the visit through verbal and nonverbal communication
2. Obtain a history through active listening and a non-judgmental, patient centered interview
3. Establish patient expectations and reason for the visit
4. Well-administered physical exam and directed investigations
5. Determine what the patients understands as the underlying cause of their condition and concerns regarding outcomes
6. Identify patient understanding of their symptoms and provide an explanation taking the patients beliefs into consideration
7. Reconcile patients' expectations on improvement and the provider's ability to help
8. Explain how stressors can impact symptoms consistent with patients' belief system
9. Set boundaries
10. Shared decision-making
11. Make treatment recommendations consistent with patient interests and beliefs
12. Establish long-term relationship with patient and primary care provider

Adapted from Drossman et al. 2016 [3]

improve patient satisfaction, adherence to treatment, and outcomes, the Rome IV Foundation created a 12-step approach to building patient-physician relationships with patients with DGBI (Table 19.2) [3].

Physical Exam

The physical exam is a rite of passage for medical professionals. The significance of a physical exam is more profound than simply the structure of the human body [40]. The human body embodies not only bones and organs but is a symbol of history, culture, and politics. The concept of embodiment rejects mind/body dualism and looks at the body as a whole situated in society to better understand how illness and pain further defines how an individual lives their human experience [40, 41]. The role of the physician in a white coat and the patient donning a gown signifies a power imbalance, allowing the physician to lie his/her hands on the body implies vulnerability and trust on behalf of the patient. These actions must be done attentively and compassionately to preserve the trust and respect of the patient and further deepen the patient-provider relationship.

The role of the physical exam is not only to diagnose a specific problem but may have a positive or negative impact on the patient depending on how it is performed. Studies completed on the placebo effect have demonstrated that it is not only the pill that is responsible for the neurobiological effects on the patient but the ritual surrounding the patient-provider encounters including positive expectations [42]. On the other hand, there can be a nocebo effect, where negative expectations may have an adverse effect on the patient [43]. Taking into consideration the placebo and nocebo effects, a physical exam administered with warmth and empathy can have a positive impact on the patient and aid in building a stronger patient-provider relationship. This can also lead to increased satisfaction and meaningfulness in the provider's practice.

Symptom-Based Approach to Functional Gastrointestinal Disorders

Over the past 30 years, the Rome Foundation has forged a path for research on FGID and developed symptom-based criteria to diagnose FGID. The Foundation has emphasized that in order to advance the field of FGID, we need to address the following: (1) the term "functional gastrointestinal disorders" lacked precision and carries some degree of stigma. (2) The diagnostic criteria are not practical in the clinical setting and lack meaningful subsets of diagnoses to identify physiological biomarkers that may lead to targeted treatment options. (3) The degree to which psychological comorbidities impact the severity of the condition, degree of disability, and centrally mediated treatment options was unclear. (4) Lack of investigative pathways to determine proper diagnostic testing based on severity and disability prior to implementing the diagnostic criteria. (5) Lack of cultural diversity in knowledge acquisition. (6) Multiple changes were made to the Rome IV diagnostic criteria released in 2016 to address previously recognized limitations including removing the term "functional" when not needed to improve specificity and decrease potential stigma associated with these conditions.

The current Rome IV diagnostic criteria are based on symptoms rather than physiological criteria, which makes them more practical for clinical use. The disorders are classified into anatomic regions, with pediatric DGBI further categorized into neonate/toddler and child/adolescent DGBI (Table 19.3) [6]. The presentation of DGBI is dependent on the age and stage of development. Functional symptoms of childhood may accompany normal development or may arise from abnormal internal or external stimuli such as the retention of feces in the rectum due to a history of painful bowel movements, which leads to maladaptive behavioral responses.

One of the limitations of using symptom-based diagnostic criteria in pediatrics is the difficulty in getting an accurate

Table 19.3 Functional GI disorders: Neonate/toddler and child/adolescent

Functional nausea and vomiting disorders
Infant regurgitation[a]
Cyclic vomiting syndrome (CVS)
Functional nausea and functional vomiting
Functional nausea
Functional vomiting
Rumination syndrome
Aerophagia
Functional abdominal pain disorders
Infant Colic[a]
Functional Dyspepsia
Postprandial distress syndrome
Epigastric pain syndrome
Irritable bowel syndrome (IBS)
IBS with predominant constipation
IBS with predominant diarrhea
IBS with mixed bowel habits
IBS unclassified
Abdominal migraine
Functional abdominal pain – NOS
Functional defecation disorders
Functional diarrhea[a]
Infant dyschezia[a]
Functional constipation
Non-retentive fecal incontinence

Adapted from Drossman et al. 2016 [6]
[a]Conditions found only in neonates and toddlers

description of the symptoms and associated triggers, especially in young children. Further, the Rome criteria alone do not address the psychological impact on illness behavior, functional disability, and severity of disease, which influence treatment and outcomes.

Prevalence

Functional gastrointestinal disorders are common disorders among children and adolescents. In a large-scale prevalence study of US children ages 4–18 years, 23.1% of the children qualified for at least one DGBI. The most common DGBI were functional constipation and abdominal migraine. Children who met the criteria for DGBI have lower quality-of-life scores than those without a DGBI. Children were also more likely to have a DGBI, if the parent also had a DGBI[44].

Functional Nausea and Vomiting Disorders

There are a spectrum of disorders that fall under this category, including cyclic vomiting syndrome (CVS) and abdominal migraines (see Chap. 28). In chronic functional nausea, the bothersome symptom is nausea, which occurs at least twice weekly for a minimum of 2 months. The symptom is generally not associated with meals or vomiting. Functional nausea can occur in conjunction with other pain-predominant DGBI. Recent data indicate a high number of comorbidities and psychosocial disability [45]. Autonomic disorders, such as POTS, are frequently associated with refractory nausea, particularly in adolescent females [10]. Family history of migraine is commonly reported. Based on clinical presentation, predominant symptoms, and severity of disability, a clinician can determine the appropriate diagnostic and treatment plan. Studies have shown that extensive diagnostic workup has a low yield in the absence of red flags [46]. With a detailed history and physical exam, diagnosis may be made prior to the recommended time frame in the Rome criteria. It is important to consider additional etiologies, which may mimic these conditions such as intestinal malrotation and ureteropelvic junction obstruction [47–50]. Treatment is phenotype specific. Although pediatric data are sparse, empiric therapy with tricyclic antidepressants and cyproheptadine at similar doses as used for CVS prophylaxis is generally first-line therapy (see Chap. 28). Other migraine agents and anticonvulsants, such as topiramate or valproic acid, can be considered, especially in refractory cases [51].

Functional Abdominal Pain Disorders

Functional abdominal pain disorders (FAPD) can be subclassified into functional dyspepsia, irritable bowel syndrome (IBS), abdominal migraine, and functional abdominal pain – not otherwise specified (FAP-NOS) depending on specific details regarding pain location, severity, quality, and associated symptoms (Table 19.3). It is important to identify any red flags such as unintentional weight loss, blood in the stools, persistent right upper or lower abdominal pain, persistent vomiting, dysphagia, odynophagia, arthritis, family history of inflammatory bowel disease, or nocturnal diarrhea which may prompt additional work or endoscopy evaluation.

Since varied factors can contribute to the development and progression of FAPD, the management of these disorders can often involve multiple treatments and should be tailored for individual patient needs based on the severity and duration of their symptoms. Management begins with a thoughtful discussion of the diagnosis and treatment options with the family and the child. The biopsychosocial model of FAPD development and tailoring treatment strategies to the individual child are important. Dietary triggers should be identified and eliminated, and cognitive behavioral therapy (CBT) has been shown to be very effective [52]. Four types of psychotherapies have been identified to be the most beneficial for patients with DGBI: cognitive behavioral therapy, psychodynamic interpersonal therapy, mindfulness/acceptance-based therapy, and gut-directed hypnotherapy [53–55].

Mild Symptoms

Patients with minor symptoms, which are infrequent, not affecting daily activities, causing psychological distress, or leading to increased visits to the doctor's office, can be managed by education, reassurance, and diet. They tend to have less psychiatric comorbidities and a better quality of life. Supplements such as peppermint oil or herbal combination preparation STW 5 (Iberogast®) have been shown to improve abdominal pain in patients with IBS and functional dyspepsia [56, 57]. A food diary may be helpful for patients to identify certain triggers leading to worse symptoms.

Moderate Symptoms

Patients who have intermittent disruptions in their daily lives, missing occasional school days, other activities, and a more frequent symptom profile with poorer quality of life require closer follow-up of symptoms and monitoring of psychological stressors. These patients would benefit from keeping a symptom diary for 1–2 weeks and associated triggers. Pharmacotherapy should be directed at the predominant symptom causing the most disruption in daily life. Asking the patient, "Of all the symptoms we discussed today, which one is the most bothersome?" is very helpful in improving patient satisfaction and outcomes. Psychological treatment should be utilized in patients who identify specific stress triggers and who are motivated to participate. Multiple therapies have been shown to decrease anxiety and improve quality-of-life measures such as cognitive behavioral therapy, mindfulness, meditation, and relaxation [34].

Severe Symptoms

Patients with severe symptoms of DGBI are best cared for by a multidisciplinary team involving psychiatry, psychology, nutrition, and gastroenterology and pain management. In addition to the gastrointestinal symptoms, these patients have significant psychological comorbidities and dysfunction in daily life and poor quality of life. They have increased psychological distress due to chronicity of their symptoms and often have comorbid psychiatric conditions such as depression and anxiety. These patients may suffer from early childhood trauma, decreased coping skills, and a poor social support system. In their previous health care experience, they may have felt stigmatized with their condition being told, "It's all in their head" and deny any potential involvement of psychosocial factors often refusing psychological and psychiatric treatments. They often seek multiple opinions with unrealistic expectations of a cure for their symptoms. Establishing a trusting patient-provider relationship is the foundation for treatment of these patients and can prevent "doctor shopping" behavior. Patients must understand that the provider is listening to their concerns and is addressing their complaints without bias. The Rome IV 12-step approach to patients withDGBI addresses the main principles in establishing a solid patient-provider relationship while improving patient satisfaction and outcomes. In addition to the 12- step approach, providers should perform diagnostic and therapeutic interventions based on objective findings rather than at the request of the patient. Predominant psychiatric comorbidities (anxiety and depression) in need of treatment should be identified and treated appropriately. The Rome IV Foundation working team published a guide on Neuromodulators for Functional Gastrointestinal Disorders (Disorders of Gut-Brain Interaction) for treatment of psychiatric comorbidities and chronic pain syndromes. See Fig. 19.2 for pharmacological treatment options [36].

Gastrointestinal tract activity is mediated through neurotransmitters and neuropeptides, which are found in both the central nervous system and the intestine. These substances can impact both human behavior and GI function. It is important to identify which areas of the brain-gut access are most affected to guide the treatment plan. As pain becomes more severe, patients may develop additional comorbidities as they suffer from chronic pain leading to the need for additional psychological and behavioral interventions. Acetylcholine is the primary excitatory neurotransmitter in the parasympathetic nervous system that drives motility in the gastrointestinal tract. Disturbances in acetylcholine secretion and metabolism can have a major impact on motility and secretion in the gut leading to gastroparesis and constipation. Sympathetic division of the autonomic nervous system participates in neuromodulation via serotonin, norepinephrine, and dopamine. They act primarily by inhibiting activity in the gastrointestinal tract by decreasing secretions, motility, and sphincter relaxation. Modulation of the serotoninergic system has been shown to affect the pain threshold in patients with DGBI.

Functional Defecation Disorders

Functional defecation disorders are the most commonly reported DGBI. Functional constipation can present as early at the neonatal period (see Chap. 27). Recognizing this condition and treating appropriately has major health care implications. In a Dutch tertiary hospital, one-fourth of children diagnosed with functional constipation continued to experience symptoms into adulthood. Risk factors for poor clinical outcomes in adulthood were identified, including late referral to a specialized clinic after failing first-line therapies [58]. Consider other conditions that may mimic functional constipation such as ultrashort segment Hirschprung disease and

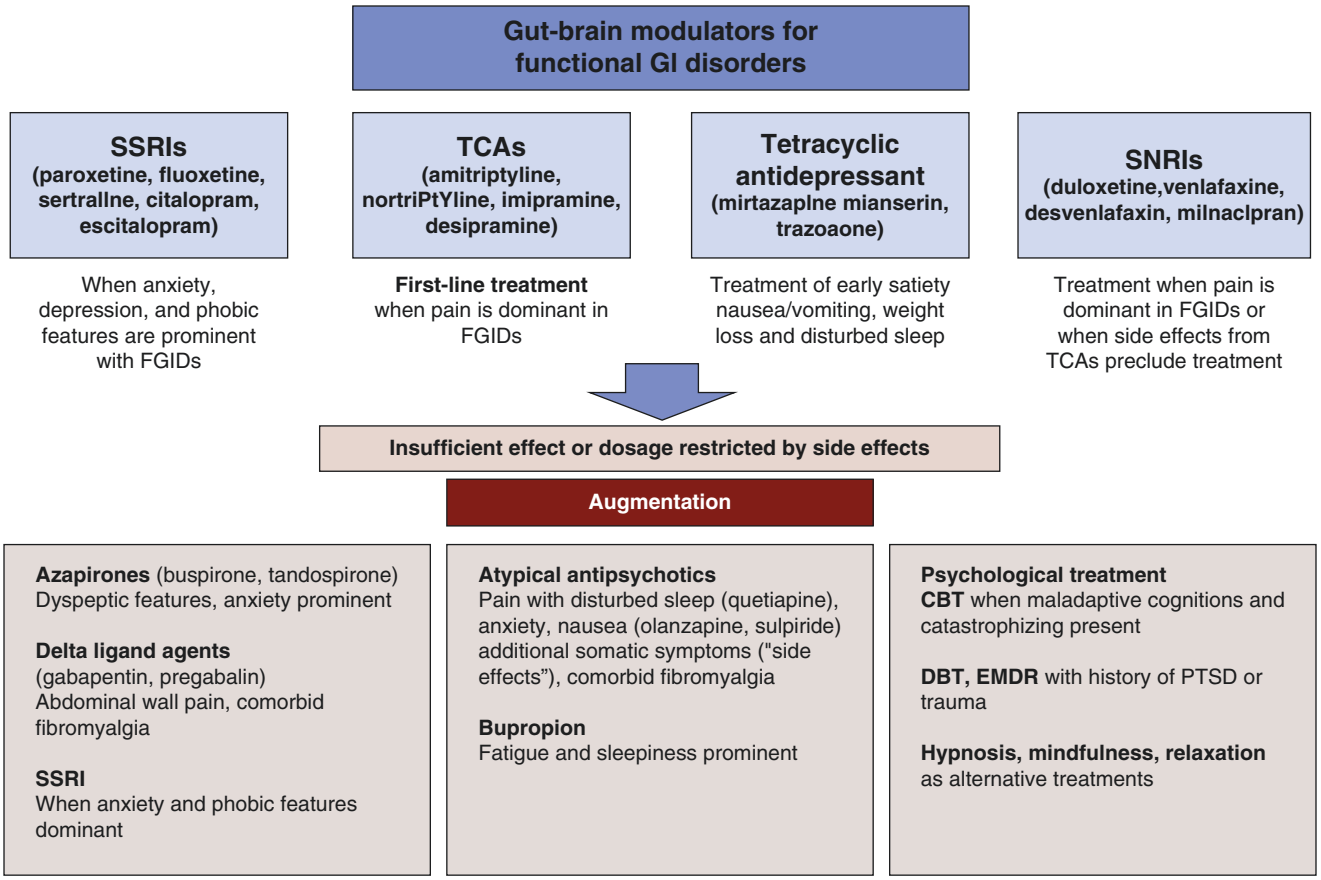

Fig. 19.2 Summary of the clinical characteristics that can be considered when selecting gut-brain neuromodulating pharmacotherapy to treat FGID. Those drugs in the upper part of the figure can be considered as first-line options. In the lower part of the figure, the pharmacologic options most often used to augment treatment effects are depicted, as well as some nonpharmacologic treatment alternatives. (DBT—dialectical behavior therapy, CBT—cognitive behavioral therapy, EMDR—eye movement desensitization and reprocessing) (Reproduced from Drossman et al. 2018 with permission from the Rome Foundation) [36]

anal stenosis in a child who presents in infancy with constipation. In addition, it is necessary to consider inflammatory conditions in toddlers who present with nonretentive fecal incontinence.

In constipation predominant irritable bowel syndrome, the lower abdominal pain persists, despite adequate laxative therapy. Soluble fiber such as methylcellulose and adequate fluid intake are generally recommended. Tricyclic antidepressants can worsen the constipation because of the anticholinergic activity, and agents with less anticholinergic activity are generally preferred for pain modulation [36].

Infant Dyschezia

Uncoordinated defecation can result in discomfort, crying, and straining in an infant. It is associated with the passage of soft stool several times a day. The disorder can be confused with functional constipation or infantile colic. The reported prevalence of dyschezia is between 0.9% and 5.6% and most infants improve by 3–6 months of age. Management involves parental reassurance and support. Overuse of laxatives or stimulants should be avoided, as they are generally not helpful. Instead, teaching the parents to flex the hips on the abdomen to relax the pelvic floor, gentle massage of the abdomen and of the perineum may help the infant to have a successful bowel movement.

Functional Diarrhea

This is characterized by passage of four or more unformed stools for ≥4 weeks with onset in infancy or preschool years in an otherwise healthy and thriving child. It is also known as Toddler diarrhea or chronic nonspecific diarrhea. Parents often report stool containing undigested food, especially vegetables like peas, carrots and corn. Rapid oro-anal transit due to immature bowel motility and excessive dietary intake of fructose, for example, fruit juices or squash have been implicated in the pathophysiology. It is important to differentiate this from malabsorption disorders and celiac disease (see Chaps. 38, 39, and 41).

Disorders of gut-brain interaction are a complex group of disorders that require a holistic approach to patient care. By taking time to listen to each patient and their story, the provider can create and long-lasting patient-provider relationship that not only improves patient outcomes but also provides meaning and satisfaction to the practice of medicine.

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