

Theoretical and Historical Basis for a Biopsychosocial Approach to Pediatric Gastrointestinal Disorders

This chapter provides a historical and theoretical context for a biopsychosocial approach to the pediatric gastrointestinal (GI) disorders. The discussion follows a progression from general mind/body issues to the specific relationship between mind/body issues in pediatric GI disorders. Then pediatric functional GI disorders are examined. Finally, the basis for pediatric GI disorders from a brain–gut axis perspective is discussed.

HISTORICAL REVIEW OF MIND/BODY RELATIONSHIP

The relationship between the mind, “psyche,” and the body, “soma,” in the causation and treatment of physical problems has a complex history in Western medicine that has yet to be satisfactorily resolved in contemporary times. Aristotle in the 4th century B.C. stated, “The body and the soul or psyche are reciprocally connected through the individual’s temperament and consequently influence each other”; separation between them does not exist (Roccatagliata, 1997).

In medieval times, the mind/body dilemma was viewed as a religious issue, and the Catholic Church institutionalized the theory of a separation of the body and the soul. The mind and the “transfer of the soul” were under the purview of the church; the body was seen as an imperfect (“sinful”) organ, a viewpoint that sanctioned the dissection of the human body. Descartes in the early 1600s proposed a model that identified differences between the mind, “res. Cognate,” a thing, which thinks, and the body, “res. Extensa,” which could be measured because it occupies space. Descartes’s theory of dualism conceptualized the human body as mechanistic and reducible to elementary parts and systems. The scientific approach to disease at this time further reinforced the notion that the body was a machine; disease was the malfunctioning of the machine. The impact of behavioral and psychosocial processes was ignored (Drossman, 1998).

During the 18th and 19th centuries the mind/body dilemma swung back and forth between an integrated concept and a dualist concept, with dualism

remaining the driving force and the dominant view. The discovery of microorganisms by Pasteur and Koch's development of the *germ theory* of disease propelled medicine toward a biomedical model (Ray, 2004). Little connection was seen between the mind and the body; illness was viewed as the result of organic pathology.

In the 20th century the issue of psychosocial versus biological influences regarding the etiology of physical problems cycled even more rapidly. In the 1920s, Flanders Dunbar (1954) introduced the term psychosomatic, which she defined as, "physical disorders, which are caused by or exacerbated by psychological factors," with the autonomic nervous system serving as the mediator between emotions and the physical responses of the body. Phenomena were observed concurrently from somatic and psychic angles, and studies examined physiological changes accompanying emotion.

Psychiatry, influenced by Freudian theory, continued to study the psychological aspects of general and specific medical problems. However, the mediator between emotions and physical illnesses was transformed into a symbolic one: unresolved dynamic emotional conflicts were associated with and thought to cause selected physical disorders such as asthma, ulcerative colitis, and peptic ulcer disease. Patients with ulcerative colitis were described as "passive, emotionally immature and pathologically attached to their mother" (Murray-Lyon & Perkin, 1998, p. 292), while children with fecal incontinence were described as "using soiling as a means of gaining attention within the context of a hostile dependency relationship with their mother" (Ringdahl, 1980, p. 65). Evidence from case reports based on descriptive observational information and correlation data was used to support the relationship between stressful life events, personality profiles, and specific organ dysfunctions or illnesses. Despite the initial wide acceptance of this theory, to date, there has been no scientific evidence that emotions "pile up" and that unresolved psychological conflicts are converted to somatic symptoms or diseases (Wilhelmsen, 2000).

In the 1960s biomedical research resulted in significant advances in the treatment of physical illnesses. The biomedical model, which originated with Pasteur, became prominent. In the biomedical model, disease is accounted for by deviations from the norm of measurable biological (somatic) variables: all biological phenomena can be explained by chemistry and physics. Disease is seen as independent of social behavior or psychological functioning, and behavioral differences are the result of disordered biochemical or neurophysiological processes and categorized as mental diseases (Ray, 2004; Entralgo, 1956).

The psychosomatic model and the biomedical model both have limitations: they are unidirectional models that are unable to account for the complex interaction of factors that impact an individual's functioning and the variety of idiosyncratic responses to physical symptoms. Neither model explains why some people with positive physical findings report feeling well, while others whose physical tests produce normal results complain of severe

pain. Although about 40% to 60% of the population has *Helicobacter pylori*, the most common cause of peptic ulcer disease (PUD) in their GI lining, only 7% of the individuals with *Helicobacter pylori* develop ulcer disease. Depression and life stressors, which increase gastric acid secretion, may increase an individual's risk. However, for some patients with PUD, emotional factors are irrelevant (Levenstein, 2000). How do we account for the variability of response to *Helicobacter pylori*?

In 1977 Engel proposed the biopsychosocial model that encompasses physical, psychological, and environmental factors and reconciles the complicated interactions and pathways among them that can lead to a disorder such as PUD (Drossman et al., 1998; Engel, 1977). This model suggests that illness, "the subjective experience of feeling unwell," and disease, "an objective biological event of either tissue damage or associated organ malfunction," result from simultaneously interacting systems at the cellular, tissue, organismal, interpersonal, and environmental levels (Drossman, 1998; Engel, 1977). The biopsychosocial model is transactional, acknowledging the reciprocal influences of both biological and psychosocial factors, and it recognizes that the boundaries between health and disease are impacted by cultural, social, and psychological considerations (Gatchel, 2004; Lamberg, 2003). This model recognizes that "feeling well" is not the same thing as being healthy; for example, a serious disease such as hypertension can be fatal with few or no symptoms. Conversely, people cannot be healthy if they do not "feel well": if someone feels pain from a misperceived normal bodily sensation, the pain still hurts regardless of the source.

Data that document the comorbidity of mental and physical health problems, especially in chronic illnesses, reinforce that physical and psychological symptoms increase together: studies have demonstrated a correlation of 0.5 between psychological distress scales and physical symptoms (Watson & Pennebaker, 1989).

THE MIND/BODY RELATIONSHIP: A HISTORY OF GASTROINTESTINAL DISORDERS

Literature documents a long history identifying the relationship between emotional factors and gastrointestinal disorders; examples from Shakespeare to the present are replete with allusions to the GI tract being affected by an array of emotions. Contemporary language confirms this association with descriptive comments such as: "gut instinct," "became choked up," "nervous stomach," and "swallowed abuse."

Early information describing the relationship between gastrointestinal functioning and emotions began with the study of individuals who had sustained a gastrostomy, the surgical construction of a permanent opening from the external surface of the abdominal wall into the stomach. Beaumont (1959), in 1833, treated a man with a permanent gastric fistula sustained by a gunshot

wound. He obtained objective data from the changes in the gastric fistula, linking emotionally charged experiences to the behavior of the stomach.

Beaumont's work stimulated further studies; Pavlov conducted perhaps the most famous of these studies, demonstrating in dogs the evoked secretory response, which occurred in anticipation of feeding. In the 1940s, Wolff conducted a case study of a man with a gastrostomy due to the burning of his esophagus at 9 years of age. Data from observations over a period of 20 years documented that his reactions to fright, depression, and being overwhelmed were associated with consistent and observable physiological changes in his stomach (Wolf, 1981). Since these earlier studies, more sophisticated neuroimaging techniques have been used to confirm the gut's responses to emotional factors (Derbyshire, 2003; Hobson & Aziz, 2004).

BIOPSYCHOSOCIAL MODEL AND PEDIATRIC GASTROINTESTINAL DISORDERS

Reports of gastrointestinal distress by children such as "my tummy hurts," "I feel like I'm going to throw up," or "I'm afraid it will hurt when I poop" are common childhood complaints voiced to parents and pediatricians. When traditional treatment methods used to manage these symptoms are not successful, the child and family are often referred to a pediatric gastroenterologist.

The problems and disorders seen in a pediatric GI practice are clinically challenging and range from the primarily functional in nature, such as recurrent abdominal pain (RAP), to those reflecting organic disease, such as Crohn's disease or ulcerative colitis. This broad range of pediatric GI problems is increasingly conceptualized from a biopsychosocial perspective. Interactions between physiological (e.g., motility, sensation) and psychological factors (e.g., life stress, emotional state, coping, social support) are seen as shaping the nature and outcome of the child's gastrointestinal symptoms. Factors such as the child's adoption of a sick role, their sensitivity to pain, their level of psychological functioning, and the family's ability to deal with the illness can all contribute to differences among children's reaction to illness (Drossman, 1998; Hyams, 1996).

Thus, for example, some adolescents with severe Crohn's disease do not limit their functioning and will not let the illness define them, participating in a wide range of academic and extracurricular activities. However, others with less severe physical symptoms but who are anxious and whose parents have significant concerns about their health status are home schooled and have little peer contact. A child with abdominal pain but with no psychosocial problems as well as good coping skills and social support will have a better outcome than the child with abdominal pain as well as coexisting emotional difficulties, high life stress, or limited support. Furthermore, the child's clinical outcome (e.g., daily function, quality of life) will, in turn, affect the severity of symptoms. This perspective stands in contrast to the conventional

medical model, which is reductionist in nature and assumes that a patient with a symptom has a disease.

The biopsychosocial model elucidates two important issues with respect to pediatric GI disorders. The first is that illness factors related to pediatric GI disorders are not the sole cause of a child or adolescent's decline in functioning: psychological and environmental factors also have an important impact on functioning. The second is that helping the child and family cope with their responses to illness-related factors (e.g., painful symptoms, diagnostic testing, and complicated treatment regimens) is important so that age-appropriate development and functioning is not impaired. Early attention to possible psychosocial contributors increases opportunities to prevent maladaptive coping, adjustment difficulties, and associated disability.

The increase in health-related quality of life (HRQOL) studies in pediatric GI disorders, (Akobeng et al., 1999; Loonen, Grootenhuis, Last, & Derkx, 2004; Pace et al., 2003; Voskuil et al., 2004; Cunningham, Drotar, Palermo McGowan, & Arendt, 2006), which assess a patient's outcome from a broader perspective than just disease measures, indicates the increasing recognition that "successful management of pediatric GI conditions should include measures of whether we improve our patient's quality of life" (Youssef, 2004, p. 461).

FUNCTIONAL GASTROINTESTINAL DISORDERS

Determining the relationship between physical and psychosocial factors is more complicated when physical symptoms such as cramping, abdominal pain, and fear of choking are present but physical findings from diagnostic tests are normal. Functional gastrointestinal disorders (FGIDs) are pediatric GI disorders in which variable combinations of chronic or recurrent GI symptoms (abdominal pain, bloating, the fear of choking, problems in the passage of food or feces, or any combination of these symptoms) predominate, but evidence of physical damage or abnormalities in the GI tract are not present (Hyams, 1999). FGIDs are linked by dysfunction of motility and in some disorders, sensory dysfunction of the gut. They exhibit shared features, including sensitivity to intestinal sensation, motility, and stress responses. From a biopsychosocial perspective, FGID symptoms represent the end product of the synthesis of a number of pathways: autonomic nervous system (ANS) reactivity and recovery, environmental stresses, the child's coping mechanisms, and parental responses to the child's symptoms.

FGIDs are prevalent and they are associated with significant work and school absenteeism, impaired HRQOL, and increased medical costs (Drossman et al., 1999; Lackner, Mesmer, Morley, Dowzer, & Hamilton, 2004; Walker, 1999). Routine activities of daily living may be curtailed for children and their families; in fact, disabilities due to FGIDs in children and for their families can equal or surpass organic GI problems, due to the uncertainty of the cause of the physical symptoms (Hyams, 1999).

Attempts to improve diagnosis and treatment of these complicated disorders have led to different conceptualizations of FGIDs. One schema is organized by focusing on issues of gastrointestinal motility, defined as the movements of the digestive system and the transit of the contents within it. Motility problems develop when nerves or muscles in any portion of the digestive tract do not function in a coordinated manner. Symptoms may range from heartburn to constipation and may also include abdominal distension, nausea, vomiting, and diarrhea (Locke, 1996).

Locke (1996) suggests that the distinctions between GI motility disorders and FGIDs are arbitrary. He proposes that motility disorders and FGIDs are not distinct diagnoses, but rather fall along a continuum, based upon the degree to which abnormal motility is thought to be involved in the pathogenesis of the disorder (Figure 2.1).

The most widely agreed-upon classification schema for pediatric FGIDs was developed in 1999 by experts in pediatric gastroenterology who met in Rome 7 years after FGIDs in adults were classified. The decision-making process for classification of pediatric FGIDs was the same as for adults: consensus for each FGID was based on clinical experience. However the classification system for children is organized by symptoms or complaints, reported by children or their parents/caregivers, whereas in adults, it is organized around targeted organs. This classification schema shifted the diagnostic process of FGIDs from an exclusionary diagnosis: the absence of organic problems, to one based upon the positive findings of specific symptoms. Consequently, the categorization of criteria for pediatric FGID's has provided

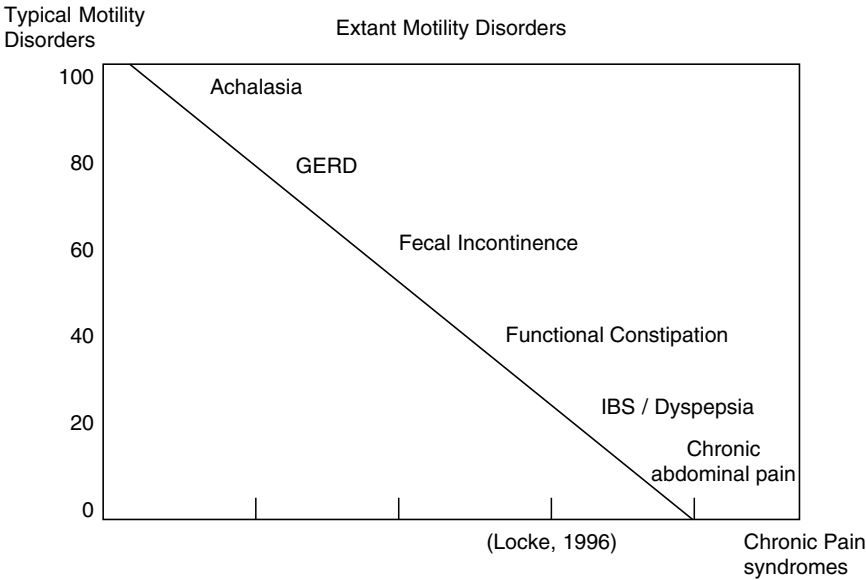


FIGURE 2.1. Extant Motility Disorders

TABLE 2.1. Classification of Functional Pediatric Gastrointestinal Disorders

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- 1. Vomiting**
 - a. Infant regurgitation
 - b. Infant rumination syndrome
 - c. Cyclic vomiting syndrome
 - 2. Abdominal pain**
 - a. Functional dyspepsia
 - b. Irritable bowel syndrome
 - c. Functional abdominal pain
 - d. Abdominal migraine
 - e. Aerophagia
 - 3. Functional diarrhea**
 - 4. Disorders of defecation**
 - a. Infant dyschezia
 - b. Functional constipation
 - c. Functional fecal retention
 - d. Nonretentive fecal soiling
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Source: Rasquin-Weber et al., 1999.

a method of standardizing FGIDs, facilitating the study of these disorders from a variety of disciplines (Table 2.1).

In children FGIDs include combinations of often age-dependent, chronic, or recurrent symptoms not explained by structural or biochemical abnormalities (Rasquin-Weber et al., 1999). Some disorders may accompany normal development such as infant regurgitation, while others may represent a maladaptive response either to internal or external stimuli, for example, fecal retention due either to a painful bowel movement (internal stimuli) or to lack of comfort using the toilet at school (external stimuli). For certain disorders including irritable bowel syndrome (IBS) and functional dyspepsia, the criteria utilized in the adult population were replicated exactly for the pediatric population because they applied equally well for children. Pediatric FGIDs that utilize the adult criteria include: globus, functional chest pain, functional heartburn, functional dysphagia, and proctalgia fugax (Rasquin-Weber et al., 1999). The Rome group recognized that the co-occurrence of a FGID and organic disease in the same child could go unrecognized. Thus a child with inflammatory bowel disease (IBD) may be overtreated because of copresenting with IBS.

The Rome group postulated that a temperament characterized in part by gastrointestinal reactivity to stress is inherited by some infants and constitutes a genetic susceptibility to FGIDs. Twin studies support an underlying genetic predisposition in those with IBS. Concordance for functional bowel disorders was 33% for monozygotic twins versus 13% for dizygotic twins (Levy et al., 2001). Two environmental factors are also reported to play a significant role in the development of FGID in children. The first is the plasticity of the neonatal brain, which may program early physiologic responses to stress during infancy and then continue into adulthood. The second factor includes illness-related behaviors and attitudes about “being sick” that children learn

from their parents or caregivers (Whitehead, 1994). Studies document that health care utilization by children closely resembles that of their parents (Schor, Starfield, Stidley, & Hankin, 1987). Levy, Whitehead, Von Korff, and Feld (2000) evaluated early learning and heritability in the clinical expression of FGIDs in childhood. They reported a relationship between a parent's response to their child's illness and a child's disability from that illness. In a more recent study, Levy (2004) found that children with higher absentee levels for GI symptoms as reported by their mothers were more likely to have parents with IBS who were more solicitous to their child's symptoms. Our clinical experience corroborates these findings. Children's symptoms can become reinforced and persist even longer when parents focus on and pay too much attention to their children's pain and illness behavior. Children with RAP, whose parents are anxious themselves and who often visit physicians, are likely to have a greater number of diagnostic procedures, inpatient hospitalizations, and outpatient doctor visits. Additionally, interference with age-appropriate functioning due to pain complaints is more likely to be tolerated. For example, if the child reports that they are "too sick to go to school," parents, with a history of anxiety, are more likely let them stay home or they will pick the child up from school if the nurse calls.

The Rome II Criteria have been instrumental in defining diagnostic categories of Pediatric FGIDs and the specific criteria of these disorders. This schema has been an important step in the development of the consensual and systematic approach to these disorders in children and adolescents. However, recently studies have indicated that the Rome II criteria may be too restrictive pertaining to the prevalence of functional disorders related to constipation (Voskuil, Heijmans, Heijmans, Taminiau, & Benninga, 2004). Efforts to validate the Pediatric Rome II criteria resulted in the development of the Questionnaire on Pediatric Gastrointestinal Symptoms (QPGS), a self-report questionnaire measuring the child's gastrointestinal symptoms (Caplan, Walker, & Rasquin, 2005). Its purpose is twofold: first, to aid pediatricians in diagnosing pediatric FGIDs and second, to serve as a research tool to estimate the incidence and the characteristics of these disorders. Further validation studies will contribute to the refinement of these diagnostic criteria and the systematic approach to these disorders in children.

It is worth noting that despite the fact that FGIDs account for the majority of visits to primary care physicians, functional gastrointestinal disorder research remains severely underfunded. Less than 1% of digestive disease research funding through the National Institutes of Health (NIH) is allocated for functional disorders (Gershon, 1998). Pace et al. (2003) cite a bias against irritable bowel syndrome (IBS), a functional disorder, considered by some physicians to be "all in the head" as compared to IBD, "a real disease," which is reflected in research funding. Despite the higher prevalence of IBS (10% of pediatric population for IBS versus pediatric data of 4.56/100,000 for Crohn's disease (CD), 2.24/100,000 for ulcerative colitis (UC), much greater resources are allocated to find a cure for IBD (Hyams, 1996; Kugathasan et al., 2003).

BRAIN-GUT INTERACTION

Studies examining FGIDs in children and adults have documented that stress and emotion impact physical symptoms in the gastrointestinal tract, from the esophagus to the rectum, and that there are intricate links between the nervous system and the digestive system (King, 2003; Pace et al., 2003; Walker, 1999; Whitehead, 1992). However, determining the pathways and the mechanisms of transmission of physical reactions to emotional situations and the reverse, emotional distress due to physical symptoms remains complicated. The conceptualization of FGIDs resulting from a brain-gut dysregulation is a hypothesis, which unifies the former dualistic concepts of mind/body issues (Wilhelmsen, 2000).

Recent progress toward a better understanding of these pathways and the transmission of information is due to two factors. First, research in the field of neurogastroenterology (the examination of the connections between the enteric nervous system and the central nervous system) has begun to delineate how these complicated pathways work and to increase our understanding of the impact of the mind/body relationship in the gastrointestinal tract. Second, there is an increase in scientific information regarding the gut's independent nervous system, the enteric nervous system (ENS).

History of Brain–Gut Interaction

The field of neurogastroenterology began with the work of Bayliss and Starling in England in the 1800s (Gershon, 1998). They isolated the intestine of a dog, stimulating the bowel from inside the intestine. Their experiments documented that digestion occurred even when the nerves to other organs in the body had been severed: the gut displayed reflex activity independent from the input of the central nervous system (CNS) (the brain and the spinal cord). They called the propulsive movement of the bowel in response to increased pressure, resulting in a coordinated wave of oral contractions and anal relaxation, the law of the intestine. In 1917, Trendelenburg (Gershon, 1998) observed the same phenomena in a loop of intestine that had been isolated from a guinea pig in an organ bath. He replaced the term law of the intestine with the term peristaltic reflex: the process by which motility in the gut proceeds without direction from the brain, spinal cord, or brainstem to the anus. Langley (Gershon, 1998), in the 1920s, described the autonomic nervous system (ANS) as a motor system of nerves that control the behavior of the visceral muscles, blood vessels, heart, and glands. He identified a third division in the ANS addition to the sympathetic and the parasympathetic, the ENS (Gershon, 1998).

The Enteric Nervous System

The ENS differs from the other two divisions in the ANS in its independence from the brain and the spinal cord. Typically commands flow from the brain via the nerves of the peripheral nervous system to muscles and glands

(the effectors that do what the brain and spinal cord tell them to do). The enteric nervous system, however, does not respond in this hierarchical function. It is an independent site of neural integration and processing, which commands the gut by processing data by itself and then acts on the basis of this data. Once food is in the stomach, digestion and absorption can take place. The CNS is needed for swallowing and defecation—in *between the gut is in charge*.

The brain and the gut originate early in embryogenesis from the same clump of tissue, which divides during fetal development. The two nervous systems, the CNS and the ENS, are connected by the longest of the cranial nerves, the vagus nerve. This large “electrical cable” extends from the brainstem through the neck to the abdomen. The enteric nervous system is located in the sheaths of tissue that surround the linings of the organs of the GI tract: the esophagus, the stomach, the small intestine, and the colon. It is composed of two networks of neural connections: the mesenteric plexus and the submucosal plexus. These two networks are closely interconnected and they have their own complex circuitry, which provides the GI tract with the means to act independently. These network circuits are responsible for providing continuous back and forth interactions of information and feedback between the gut and the brain, thereby influencing brain and gut processes and gut functions (Blakeslee, 1996).

How the Brain-Gut Axis Works

The term brain-gut axis is used to explain the bidirectional neural pathways between the cognitive and emotional centers in the brain and the enteric nervous system in the gut (Buldavari & Olden, 2003). This bidirectional communication of a constant stream of chemical and electrical messages between the CNS and the ENS is increasingly acknowledged as the underlying pathomechanism of FGIDs (Gershon, 1998.) Chronic GI symptoms are a result of the integration of intestinal, motor, sensory, autonomic, and CNS activity, which interact at all levels of the brain-gut axis (Figure 2.2).

How does this process work? Because of the neural connections from the brain, circuits can be activated by external stimuli (a frightening event, stress, reactions to smell) or internal stimuli (bad thoughts or emotions), which can then alter motility and sensation in the gut. Because of the bidirectional nature of the brain-gut axis, the effect can work in reverse: the ENS sends signals to the brain as to what is occurring in the gut. Thus, physiological disturbances in the gut can affect mood, pain perception, and behavior.

How does the transmission of information actually occur? Communication between nerve cells is the basis of functioning for any part of the vertebrate system. The components of this processing system include neurotransmitters, hormones, and cytokines that act as messenger molecules carrying information between the nervous endocrine and immune systems. Information is passed from one site to another at the synapse level with the aid of neurotransmitters. The flow of information going from the brain to the gut and the gut to the brain is regulated by a variety of neurotransmitters

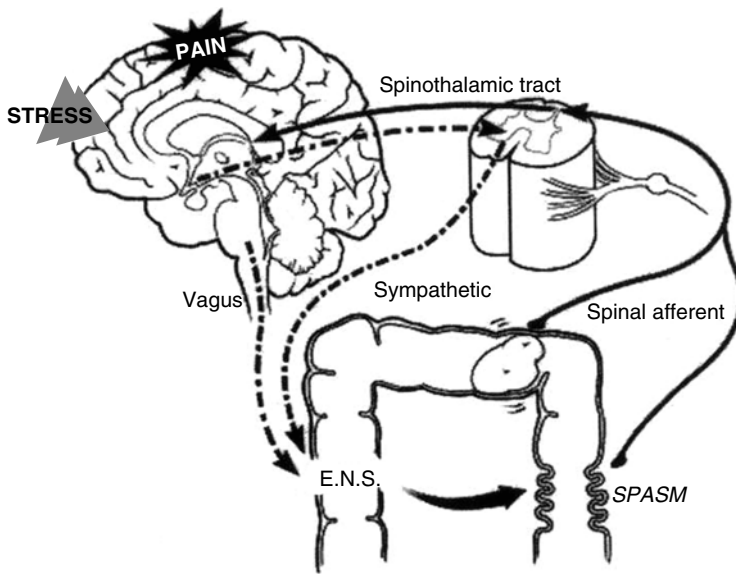


FIGURE 2.2. Brain-gut axis mechanism (Mertz, 2003)

found in both the brain and the gut. Serotonin, a brain neurotransmitter and a mediator of the brain-gut connection, is used as an antidepressant in a class of drugs called SSRIs (selective serotonin reuptake inhibitors). These drugs are thought to ease depression by increasing the amount of serotonin in the brain, yet 95% of the body's serotonin is stored and manufactured in the bowel (Kim & Camilleri, 2000). Does this class of drugs actually work on the gut, not the brain, to improve mood?

New diagnostic procedures have aided in the confirmation of this brain-gut link. Neuroimaging procedures such as computed tomography (CT) scan, positron emission tomography (PET), and functional magnetic resonance imaging (fMRI) are noninvasive imaging techniques used to examine how specific areas of the brain perform in response to visceral sensation (Derbyshire, 2003). This technology has clarified the relationship between specific regions of the brain and the functions they perform in response to stimuli.

The Brain-Gut Interaction and Irritable Bowel Syndrome

Recent research by Hamaguchi et al. (2004) supports a brain-gut relationship as a major factor in the pathophysiology of IBS. They reported findings of distension of the descending colon, which induces visceral perception and emotion, and correlates significantly with activation of specific regions of the brain including the limbic system and the association cortex, especially the prefrontal cortex. Their findings indicate that the brain has a specific functional module for response to visceral perception and perception-related emotion. Budavari and Olden (2003) suggest that variable influences of stress on

gut function as mediated through neurotransmitter release may explain varied presentations of IBS. Studies using fMRI show that people with IBS process pain differently from controls: painful rectal distension prompts greater activation of their anterior cingulate cortex, a critical pain center.

Children and adolescents with IBS have visceral hypersensitivity, a heightened sensitivity of the nerves that go from the colon to the spinal cord. They may perceive colonic sensations differently from those children without IBS. For example, they may complain of incomplete evacuation even though their rectum is empty, or they may feel distended with gas even though when measured there is no significant increase in gas. Children with IBS may have fears in the morning about exams or social issues, which can precipitate cramping or just abnormal visceral sensitivity to normal bodily functions. Their cramping causes anxiety about having to go to school: What if they have excess flatulence? What if they have to use the toilet? These concerns can lead to school avoidance, which then increases the child's feelings of pressure because of being behind in classes. Mach (2004) reported that to date scientific evidence supporting traditional therapies have been limited and that understanding the brain–gut axis is crucial in the development of new effective therapies in the management for IBS.

Figure 2.3 is a visual representation of a biopsychosocial approach to IBS, which encompasses the transactional relationship between the CNS and the ENS. This model integrates factors that lead to IBS and the transactional

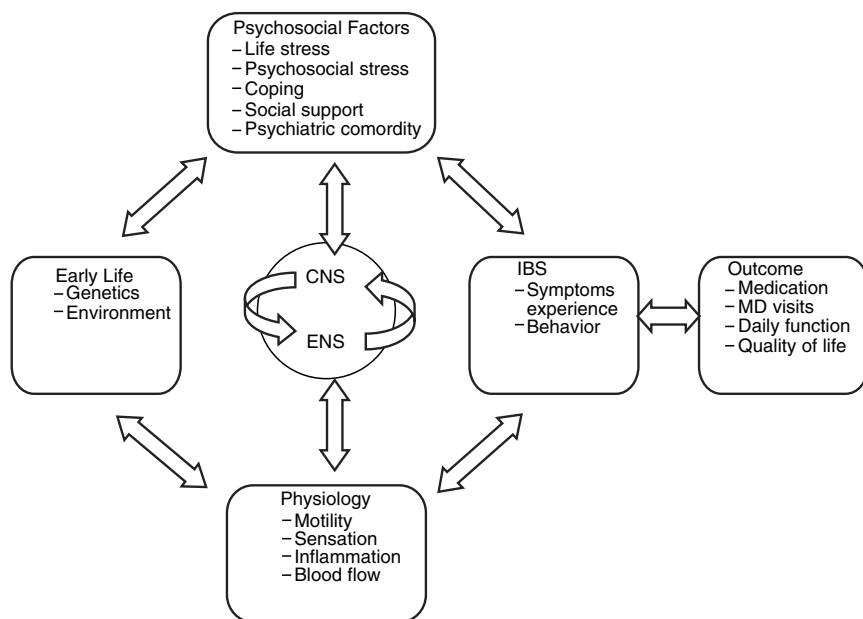


FIGURE 2.3. Biopsychosocial model of IBS depicting the relationship between early life, psychological factors, physiology, subjective experience ENS-enteric nervous system (Mulak & Bonaz, 2004)

process by which these factors affect each other, resulting in the expression of IBS in the child or adolescent. Early life factors (e.g., genetic predisposition to GI disorders) interact with physiological factors (e.g., increased visceral sensitivity in the colon, diarrhea, and cramping) and psychosocial factors (e.g., stresses such as academic and social pressures, family conflicts, comorbid anxiety) to contribute to the diagnosis of IBS. A significant feature of this schema is the outcome: How do the child and the families react once a diagnosis of IBS is made? Is IBS the focus of the child's and the family's home life? Are daily age-appropriate activities such as school, athletics, and sleepovers limited because of fears of cramping, possible incontinence, or worries about vomiting? Does the child then limit his or her functioning in response to these physical concerns? Does the child sense the parent's anxiety and then become anxious? The transactional aspect of this process is critical and unique to each child or adolescent.

This bidirectional neural pathway between the CNS and the ENS affects children and adolescents with the whole spectrum of GI disorders. King (2003) reported that the reciprocal brain-gut relationship is also seen in children and adolescents with IBD. He reported that in one direction, stress can affect physical symptoms and in the other direction, he stated that having IBD and thoughts associated with the treatment and the symptoms can impact mood.

The brain-gut theory has sparked interest as well as controversy regarding the relationship between GI symptoms and autism, a life long disorder characterized by problems with communication, socialization, and abnormal responses to sensations, including pain. For a long time, GI symptoms in children with autism had been overlooked or attributed to the behaviors (aching, flailing, and biting) and sensory dysfunction associated with autism. While parental reports, case studies, and small uncontrolled trials have reported a relationship between GI issues in children and autism, research has documented mixed results. (Erickson et al., 2005).

Several population studies have examined the prevalence of GI symptoms in children with autism. Studies report that 46–76% of children with autism have overt GI symptoms compared to 10–30% of typically developing developmentally pediatric controls (Horvath & Perman, 2002; Wakefield, 2002). The most commonly reported symptoms include chronic diarrhea, constipation, abdominal bloating, food sensitivities, and food regurgitation (Wakefield, 2002; Molloy et al., 2003). Horvath (1999) and Kushak (2002) also have documented an increase in the incidence of lactose and sugar intolerances in children with autism as compared to controls.

The history linking autism and GI disorders began with the original description of autism by Kanner (1943), who reported that 6 of the 11 children identified with this disorder had feeding difficulties. In the 1950s and 1960s, researchers evaluated diet and food allergies as a trigger for autism. Studies by Prugh (1951), Daynes (1951), and Asperger (1961) identified abnormal behaviors in children with gluten sensitivity or celiac sprue. Early studies by Crook (1961) reported cases of profound neurological behaviors including autism, which resolved with dietary changes, suggesting food allergies as

a contributory factor. Goodwin (1971) described improvements in the EEG studies of randomly selected children with autism when the children were placed on gluten-free diets. These earlier studies, however, were based on case reports and anecdotal descriptions.

Several hypotheses have been proposed to explain the linkage between the GI tract and the brain in children with autism. These include the opioid theory, irregular secretin levels, and autoimmune dysfunction. The opioid theory asserts that autism is the result of a metabolic disorder (Shattock, 1990; Reichelt, 1991), in which peptides derived from dietary sources, in particular foods that contain gluten and casein, are mixed with digestive enzymes, resulting in opioid peptides. These peptides pass through an abnormally permeable intestinal membrane ("leaky gut") and enter the CNS, causing neurological dysfunction or encephalopathic issues. Yet, in contrast to the large amount of parental anecdotal information and case studies, Erickson et al. (2005) in a review report that "overall studies analyzing the response of autistic children to dietary proteins have found mixed results" (p. 21).

Secretin has also been reported as a possible link to the GI-autism issue. Horvath et al. (1998) documented the improvement in three children with autism with respect to their GI issues as well as their eye contact, alertness, and expressive language after receiving IV secretin during a GI procedure. They hypothesized that the low level of secretin, which has an effect on gastric secretion, contributed to an increased incidence of acid reflux and perhaps pain-related behaviors. However, further studies that examined providing IV secretion to children with autism have not resulted in improvement in GI symptoms or autistic behaviors (White, 2003).

Recently studies have examined the histopathology of the GI tract in children with autism. These studies support the presence of chronic inflammation in the GI tract with the possibility of an autoimmune process contributing to the inflammatory response. Wakefield et al. (2000) undertook a systematic evaluation of GI symptoms in children with autism. Colonoscopy revealed that 93% of the children had ileo lymphoid nodular hyperplasia. Furante (2001), Torrente (2002), and Ashwood (2004) have reported immune abnormalities and abnormal cytokine profiles, inflammatory markers in children with autism who have GI symptoms. Jyonouchi, Greg, Ruby, Reddy, and Zimmerman-Bier (2005) documented a defect of innate immune responses in children with autism with GI symptoms but not in children with nonallergic food hypersensitivity or children with autism without GI symptoms, suggesting a possible link between GI and behavioral symptoms mediated by innate immune abnormalities. This subgroup of children with autism and GI symptoms may not be able to resist exposure to benign dietary triggers, which may increase behavioral symptoms.

Attempts to further understand the connections between children with autism who have GI symptoms have led to identifying different subgroups among this population. D'Eufemia et al. (1996) reported that 43% of children with autism tested had increased gut permeability but no history of GI symptoms. Molloy and Manning-Courtney (2003) found that in a study of a general

population of children with autism, 24% had a history of one chronic GI symptom, most commonly diarrhea (21%). Molloy and Manning-Courtney (2003) speculated that these children might represent a distinct phenotypic subgroup within the larger group of children who meet the criteria for autism. In light of D'Eufemia's findings, they propose a continuum of children with autism and presenting GI symptoms to include normal/ asymptomatic to abnormal/asymptomatic to abnormal/symptomatic as a paradigm for differentiating among subtypes of children with autism who have GI issues.

To date, research and parental report document that GI symptoms in certain subgroups of children with autism exist; however, a causative relationship has not been empirically documented. Behaviors associated with autism may have a variety of origins: attention seeking, self stimulation, frustration with inability to communicate, and pain that may have medical underpinnings. GI issues may exacerbate autistic symptoms; thus the treatment of GI issues may not only heal the GI symptoms but may also decrease problem behaviors in children with autism. As research continues to clarify the brain-gut connection in children with autism, GI symptoms in this population need to be carefully evaluated and treated.

In the process of examining a theoretical basis for pediatric GI disorders we have come full circle: from the Greek theory of holos (integration of psyche and soma) to dualist conceptualizations of illness, and finally to examining the brain-gut axis as a unifying principle. We end this chapter with a prescient quote from an 18th-century physician and chemist:

Finally the mind itself and the body, things generally held to be of entirely disparate nature, are so tightly and intimately knit when joined together in man that—if I may here speak as a chemist—they interpenetrate and dissolve in each other, so that while life flourishes, wherever there is mind there is body, and wherever body, mind. There is hardly to be found any smallest part of man in which something of the mind and something of the body, and in measure a mixture of both, is not to be observed. (Jacob Gaub, in Rather, p. 34, 1965).

Simply put, the brain affects the gut and the gut can affect the brain.

The following chapters focus on the assessment and treatment of the following pediatric gastrointestinal disorders: inflammatory bowel disease (IBD), recurrent abdominal pain (RAP), vomiting disorders, esophageal disorders (globus sensation, gastroesophageal reflux (GER), gastroesophageal reflux disease (GERD), irritable bowel syndrome (IBS), and defecation disorders. For each of the disorders discussed, we will present:

1. Our clinical experience in terms of assessing and treating these disorders.
2. What we know from evidenced-based research about the treatment of these disorders. What data report regarding which psychosocial treatments work best with which pediatric GI disorder.
3. The roadblocks in treating these pediatric GI disorders from a biopsychosocial perspective.

Our goal is to clarify what is known with respect to the psychological and behavioral assessment and treatment of pediatric GI disorders and to elucidate the areas in need of further investigation.

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