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SPECIAL ARTICLE

A Rome Working Team Report on Brain-Gut Behavior Therapies for Disorders of Gut-Brain Interaction

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BACKGROUND AND AIMS: This Rome Foundation Working Team Report reflects the consensus of an international interdisciplinary team of experts regarding the use of behavioral interventions, specifically brain-gut behavior therapies (BGBTs), in patients with disorders of gut-brain interaction (DGBIs). **METHODS:** The committee members reviewed the extant scientific literature and, when possible, addressed gaps in this literature through the lens of their clinical and scientific expertise. The Delphi method was used to create consensus on the goals, structure, and framework before writing the report. The report is broken into 5 parts: 1) definition and evidence for BGBT, 2) the gut-brain axis as the mechanistic basis for BGBT, 3) targets of BGBTs, 4) common and unique therapeutic techniques seen in BGBT, and 5) who and how to refer for BGBT. **RESULTS:** We chose to not only review for the reader the 5 existing classes of BGBT and their evidence, but to connect DGBI-specific behavioral targets and techniques as they relate directly, or in some cases indirectly, to the gut-brain axis. In doing so, we expect to increase gastrointestinal providers' confidence in identifying and referring appropriate candidates for BGBT and to support clinical decision making for mental health professionals providing BGBT. **CONCLUSIONS:** Both gastrointestinal medical providers and behavioral health providers have an opportunity to optimize care for DGBIs through a collaborative integrated approach that begins with an effective patient-provider relationship, thoughtful communication about the brain-gut axis and, when appropriate, a well communicated referral to BGBT.

Keywords: Gut-brain axis; irritable bowel syndrome; behavioral interventions; gut-directed hypnotherapy; cognitive behavior therapy.

This Rome Foundation Working Team Report (WTR) reflects a review of the scientific evidence and consensus (Delphi method) of an international interdisciplinary team of experts in psychophysiology and neuroscience, behavioral intervention science, nursing and symptom science, and gastroenterology. The committee consisted of 4 practicing academic gastrointestinal (GI) psychologists representing the broader consensus of the Rome Foundation's GastroPsych Division, which is responsible for the training and continuing education of mental health specialists in disorders of gut-brain interaction (DGBIs). The WTR was assembled to determine the role of behavioral interventions in the management of DGBIs. Consistent with the Rome Foundation's new definitional guidelines, these behavioral interventions have been renamed brain-gut behavior therapies (BGBTs) to reflect their focus on improving GI symptoms and evidence that they do indeed target specific cognitive, emotional, and behavioral mediators associated with gut-brain dysregulation. Furthermore, we expect the term to be less stigmatizing and increase acceptance of the use of behavioral treatments as part of integrated care for digestive disorders. Clinical pearls and resources are included throughout.

Methods

Our committee reviewed the extant scientific literature and, when possible, addressed gaps in this literature through the lens of their clinical and scientific expertise. This process occurred from January 2020 to October 2020 through a series of video calls and e-mail exchanges. Delphi methodology was used to create consensus on the goals of the WTR, theoretical framework, and level of detail for each content area before writing the report. The committee decided that while it was important to review for the reader the 5 existing classes of BGBT and their evidence, this has been recently done.[1–3] The team decided to focus the report on the connection of DGBI-specific behavioral targets and techniques as they relate directly, or in some cases indirectly, to the gut-brain axis. It is our view that although GI providers are increasingly aware of BGBTs and their evidence, they may be less familiar with the behavioral targets and techniques that comprise these interventions, how BGBTs are similar or different from each

Abbreviations used in this paper: **BGBT, brain-gut behavior therapy; CBT, cognitive behavioral therapy; DGBI, disorder of gut-brain interaction; IBS, irritable bowel syndrome; RCT, randomized controlled trial; WTR, Working Team Report.**

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WHAT YOU NEED TO KNOW

BACKGROUND AND CONTEXT

There is a growing need for gastroenterologists to understand both the theoretical and the practical aspects of brain-gut behavior therapies (BGBTs) as part of integrated care for digestive disorders.

NEW FINDINGS

The international Rome Foundation Working Team reviews the strong evidence behind existing and emerging classes of BGBT and, for the first time, provides the framework for a gastrointestinal provider to understand the BGBTs' specific behavioral targets and techniques as they are applied to patients with disorders of gut-brain interaction.

LIMITATIONS

The reader is strongly encouraged to seek out additional information from the resources provided within the paper.

IMPACT

The goal of this paper was to empower gastrointestinal providers to thoughtfully communicate, when appropriate, the scientific rationale and a clear pathway for engaging with a BGBT as part of integrated care.

other, or how BGBTs differ from other forms of psychotherapy. To achieve this, the report was broken into 5 parts: 1) definition and evidence for BGBT, 2) the gut-brain axis as the mechanistic basis for BGBT, 3) targets of BGBT, 4) common and unique therapeutic techniques seen in BGBT, and 5) who and how to refer. Writing began in November 2020 and underwent several iterations. We hope this report will increase GI providers' confidence in identifying and referring appropriate candidates for BGBT and further support clinical decision making for mental health professionals providing BGBT.

Section I. Definition and Evidence for BGBT

BGBTs are clinician administered, short-term, nonpharmacologic interventions that prioritize the remediation of GI symptoms over improvement of psychological comorbidity, although the latter is also possible. As such, BGBT can be highly personalized, and include a combination of effective techniques that draw from the extant behavioral intervention literature. BGBT can also be combined with other behavioral therapies, and when needed, with neuromodulators[4] and is an important part of integrated care for DGBIs.[2] BGBT is typically offered in conjunction with medical therapies and only rarely serve as stand-alone "alternatives" to medical care, although certainly these interventions may be offered as stand-alone if this is the patient's and provider's shared preference. Because most BGBTs work at central or gut-brain systems of symptom control, their effects do not need to be condition or symptom specific. One exception to this approach is the efficacy for rectal biofeedback, a behavioral technique, that is not necessarily considered a class of BGBT by the Working Team, but can be used as primary treatment for problems such as fecal incontinence or dyssnergic defecation.[5,6] Therefore, although the scientific literature is limited to studying patients with irritable bowel syndrome (IBS), dyspepsia, or other more common DGBIs, our expert consensus is that the benefit of BGBT will be clinically realized across the spectrum of DGBIs and structural disorders, and future studies will seek to determine this.

In this section, we briefly review each of the existing evidence-based categories of BGBT and, when possible, provide data on potential mediators of outcome: 1) self-management programs, 2) GI-focused cognitive-behavioral therapy (CBT), 3) gut-directed hypnotherapy, 4) mindfulness-based interventions, and 5) psychodynamic-interpersonal therapy (Table 1).

DGBI Self-Management Programs

Disease self-management programs are rooted in the belief that self-efficacy, or confidence in one's ability to manage one's health, is critical to improving GI symptoms, psychological symptoms, extraintestinal symptoms, and health-related quality of life in patients with DGBIs.[7–11] Many of these programs can be delivered in the form of self-help workbooks.[10,12] Self-management training can contribute to a reduction of disease-related anxiety and correction of common misconceptions about DGBIs, and to increased awareness of common symptom triggers, such as diet, stress, and physical activity, which can lead to improved self-confidence, self-care, and hope.[13] Stress management is often a significant component of self-management training programs, given the impact of stress on DGBI symptoms and symptom perception. Self-management programs are considered to be cost saving compared with other kinds of therapy that require more intensive resources,[12] and they can be delivered telephonically or online.[8,14] In the majority of studies on self-management interventions, delivery is by or with the support of nurses or nurse educators.[7,11,15,16]

Cognitive-Behavioral Therapy

CBT is rooted in the belief that thoughts, feelings, and behaviors are interconnected and can become maladaptive through learned experiences. CBT focuses on the unlearning of maladaptive coping skills that have developed as a response to GI symptoms and/or stress, and can also address previous learned behaviors or coping skills that may have increased a patient's risk for developing a DGBI. CBT is one of the most well tested BGBTs for DGBIs, with more than 30 randomized controlled trials (RCTs) supporting its use in multiple forms of delivery, including group based, internet delivered, and with minimal therapist contact.[17] Systematic reviews and network meta-analyses of CBT demonstrate short and long-term symptom improvement in IBS,[18] and smaller RCTs demonstrate efficacy of CBT for non-cardiac chest pain[19] and dyspepsia.[20] Studies that have investigated potential mechanisms of change in CBT trials for IBS suggest that change in illness-specific cognitions and avoidance behavior, rather than change in general anxiety or stress, mediates treatment effects on IBS symptom severity.[21,22] Minimal therapist contact interventions might address traditional barriers for psychological therapy from the

Table 1. Brain-Gut Behavior Therapies: Theory, Targets and Techniques and Evidence Base

	Disease self-management	Cognitive behavior therapy	Gut-directed hypnotherapy	Mindfulness-based stress reduction	Psychodynamic interpersonal psychotherapy
Theoretical framework	Empowering patients to be active participants in their care through disease knowledge and lifestyle (sleep, diet, activity)	Thoughts, feelings, and behaviors are learned and influence symptom and symptom perception.	Heightened state of focus and awareness can increase openness to suggestions for change.	Being grounded in the moment and recognizing that while pain may be inevitable, suffering can be decreased, reducing physical vulnerability to stress.	A strong, trusting and collaborative relationship can lead to change.
Brain-gut targets	Psychological stress	Psychological stress, negative emotion, maladaptive cognitive processes, avoidance, psychological comorbidity, somatization, abuse and early-life experiences	Psychological stress, maladaptive cognitive processes, somatization	Psychological stress, negative emotion	Negative emotion, abuse and early-life experiences
Common techniques[a]	Stress management, relaxation training	Stress management, relaxation training	Relaxation training, autogenics	Relaxation training	Psychoeducation
Specific techniques	None	Exposure, cognitive restructuring, flexible coping training, mindfulness practice	Post-hypnotic suggestions	Mindfulness practice	
Type of provider	Any	Mental health professional only	Specialty training	Specialty training	Mental health professional only
Evidence base[b]	Effective in RCTs for IBS	Effective in meta-analyses for IBS, effective in RCTs for FD, NCCP	Effective in meta-analyses for IBS, effective in RCTs for FD, NCCP, duodenal ulcers, functional abdominal pain, effective in case series in reflux and globus	Effective in 3 RCTs in IBS	Effective in meta-analyses for functional somatic syndromes, effective in RCTs in IBS and FD
Alternative delivery methods	Self-help workbooks, groups, online, telephone	Self-help workbooks, groups, online, telephone, digital	Groups, online, digital	Groups, online	None known

Table 1. Continued

	Disease self-management	Cognitive behavior therapy	Gut-directed hypnotherapy	Mindfulness-based stress reduction	Psychodynamic interpersonal psychotherapy
Preferred patient population	Mild symptoms, limited psychological distress	Moderate to severe symptoms, evidence of fear, avoidance or maladaptive cognitions; some may target psychological insight and flexibility[c]	Severe to refractory symptoms, high levels of somatization, no unresolved abuse history or dissociative disorders (PTSD, borderline PD)	Mild to moderate symptoms, comorbid PTSD; most data in women or veterans	Severe to refractory symptoms, somatization, interpersonal difficulties, trauma history

FD, functional dyspepsia; IBS, irritable bowel syndrome; NCCP, non-cardiac chest pain; PD, panic disorder; PTSD, post-traumatic stress disorder; RCT, randomized controlled trial.
[a]All brain-gut behavior therapy classes include an effective patient-provider relationship and psychoeducation, so these are not listed here.
[b]It is important to note that low levels of evidence supporting brain-gut behavior therapy in recent clinical guidelines are due to the evaluation of brain-gut behavior therapies in the same manner as pharmacological trials. Future research should incorporate alternate methods to the evaluation of rigor, which will likely increase the evidence supporting BGP and lead to more nuanced recommendations. For additional reading into the importance of mind-body approaches in health care, we recommend Dossett ML, et al. A new era for mind-body medicine. N Engl J Med 2020;382:1390–1391.
[c]Contextually based cognitive behavioral therapies, including acceptance and commitment therapy are often recommended for patients with chronic pain and for whom psychological flexibility is limited, with growing data supporting its use in disorders of gut-brain interaction.

patients' perspective and seem to be as effective, even in the long term, as traditional therapist-delivered therapy.[9,23] CBT may be delivered in person by trained providers, usually by mental health professionals, but telephonic, online, and digital applications of CBT for IBS are increasingly available, with or without nurse support,[8,14] and are an area of future study.

Contextually based behavior therapies. Though less studied in DGBI, contextually based CBT approaches such as acceptance and commitment therapy, dialectical behavior therapy, mindfulness-based cognitive therapy, and behavioral activation are of growing interest and align well with the therapeutic targets of BGBT. These approaches de-emphasize the content of thoughts and rather seek to build and broaden psychological flexibility and a repertoire of new behaviors that are consistent with a patient's values, as reviews by Sebastian Sanchez et al.[24] The Working Team hypothesized that contextually based behavior therapies, particularly acceptance and commitment therapy, are likely to become BGBTs as data continues to accumulate.

Gut-Directed Hypnotherapy

Gut-directed hypnotherapy is a form of medical hypnosis provided by a specially trained clinician. DGBI patients are placed into a heightened state of focus and awareness to increase openness to post-hypnotic suggestions. Suggestions are customized to the patient's symptom profile, but usually focus on broader themes of gut-brain dysregulation. There is evidence from systematic reviews and meta-analyses for efficacy in IBS,[25–27] evidence from smaller RCTs in functional abdominal pain, dyspepsia, duodenal ulcers, non-cardiac chest pain, and ulcerative colitis,[28] and evidence from case series reports in globus[29] and reflux.[28] There is evidence that hypnosis may improve symptoms through normalization of visceral sensitivity, motility,[30] and to some extent maladaptive cognitions and extra-intestinal manifestations of DGBI.[31,32] Gut-directed hypnotherapy can be successfully delivered via groups[33] and video calls,[34] and digital options are emerging on the market as well.

Mindfulness-Based Interventions

Mindfulness-based interventions have shown effectiveness for a wide range of psychological and medical conditions and are rooted in the belief that being grounded in the moment, accepting pain as inevitable, can reduce suffering and stress and improve emotion regulation.[35,36] Mindfulness practice is relevant to DGBIs owing to their stress-sensitive nature, and learning how to stay grounded or calm in the moment when encountering stressful situations can decrease symptoms.[37] In IBS, mindfulness-based stress reduction has been shown to improve specific symptoms such as constipation, diarrhea, bloating, and GI-specific anxiety in RCTs.[38–40] Furthermore, mindfulness can decrease visceral hypersensitivity and improve cognitive appraisal of symptoms, resulting in improved quality of life.[41] A range of professionals can be trained in mindfulness, and community group-based mindfulness programs are often available.

Psychodynamic-Interpersonal Therapy

Psychodynamic-interpersonal therapy is a BGBT offered by a highly trained psychotherapist and rooted in the belief that a strong, trusting, and collaborative relationship is a primary vehicle of change. Through this relationship, the patient will be able to repair negative emotions driving their DGBI symptom experience. Psychodynamic-interpersonal therapy is often recommended for patients with severe persistent symptoms whose illness identity and associated interpersonal difficulties have become a primary focus in life.[42] Meta-analyses have shown effectiveness of psychodynamic-interpersonal therapy for functional somatic syndromes,[43] as have RCTs in IBS and dyspepsia.[44,45] Furthermore, there is evidence that psychodynamic-interpersonal therapy is superior to paroxetine and cost-effective.[46] Psychodynamic-interpersonal therapy is particularly effective in cases of trauma or early life adversity.[47] It may also work through continued exposure to negative emotions, as in CBT.

Clinical Connection:
Though the reader may be familiar with many of these interventions for a range of medical and emotional disorders, it is important to be able to explain to patients that these behavior therapies are called BGBTs for 2 very specific reasons: 1) they address the modifiable factors underlying gut-brain dysregulation, and 2) they have been modified from traditional uses to specifically address the concerns of patients with DGBIs. For further information on these therapies and approaches, especially if you are a mental health provider, see Knowles SR, Keefer L, Mikocka-Walus AA. Psychogastroenterology for adults: a handbook for mental health professionals. London & New York: Routledge/Taylor & Francis Group, 2020.

Section II. What Makes a BGBT a BGBT? The Gut-Brain Axis as the Mechanistic Basis for BGBT

The bidirectional interconnections between the gut and the brain constitute the fundamental conceptual and mechanistic basis for the use of BGBT in DGBIs, and behavioral targets and techniques that are both common and specific to each BGBT have been carefully chosen based on the general framework of the gut-brain axis. Although mechanistic details on the pathways and mediators of the gut-brain axis are out of the scope of this WTR, in this section we provide a general description of its most prominent components with the use of relatively general terms that could also be helpful to explain to patients that BGBTs have a sound scientific and mechanistic basis.

The gut-brain axis is composed of multiple communication pathways that connect the brain with the gut. These pathways are increasingly well characterized, the underlying biological and physiological mechanisms are the subject of intense translational research in animal models, healthy humans, and patients, and knowledge about functional changes in DGBIs continuously evolve. In principle, afferent (gut-to-brain) pathways transmit information from sensory receptors in visceral GI organs to the brain where cognitive, emotional, and behavioral responses are orchestrated. Understanding the peripheral (inflammation, injury) and central (cognitive, affective) mechanisms underlying normal and heightened viscerioception (perception of sensations arising from organs) is important to be able to explain to a patient how visceral perception can become altered in patients with DGBIs.[48,49] Among the sensations that induce suffering and constitute behavioral treatment targets in patients, visceral pain is most prominent. However, other common GI symptoms, including nausea, distension, fullness, bloating, abdominal cramping, and discomfort are also clinically relevant and involve similar perceptual alterations along the gut-brain axis, in line with the prominent role of visceral hypersensitivity in GI symptom generation.[50]

Clinically, one could explain that the communication pathways from the gut to the brain in DGBI patients experiencing visceral pain are more easily activated and transmit information more readily, and that visceral sensory input is preferentially processed within the brain, ultimately resulting in greater perceived pain intensity and/or unpleasantness and physiological responses.

The brain processing of sensory information arising from the viscera involves multiple subcortical and cortical brain regions[51] and is referred to as central mediation or central processing. Central processing of gut sensations has been extensively studied with the use of brain imaging techniques in humans, especially in the context of painful sensations arising from the esophagus, stomach, and rectum, and is consistently found to be altered in patients with DGBIs compared with healthy control subjects.[51] Since the experience of pain is characterized not only by sensory but also by complex emotional and cognitive facets, it is not surprising that altered brain processing in patients engages not just multiple brain regions, but rather interconnected brain networks, including sensorimotor, emotional arousal, and salience networks. The structure and function of these brain networks is modulated by central stress-sensitive pathways, including the corticotropin/corticotropin-releasing factor pathways and the locus ceruleus/noradrenergic pathways that also link with efferent components of the gut-brain axis (see below).

Of note, the brain processing of visceral pain appears to be at least partly distinct from the brain processing of somatic pain.[52,53] This could be due to specific afferent sensory pathways, but also related to the emotional properties of interoceptive visceral sensations, which are much more diffuse, but highly unpleasant, and can evoke aversive psychological experiences that are highly modifiable by emotional and cognitive factors. These emotional properties are some of the most well studied therapeutic targets of BGBT.

Finally, as key component of efferent (brain-to-gut) pathways, the GI tract with its enteric nervous system is innervated by the autonomic nervous system, providing one of the efferent pathways that links the brain's response to

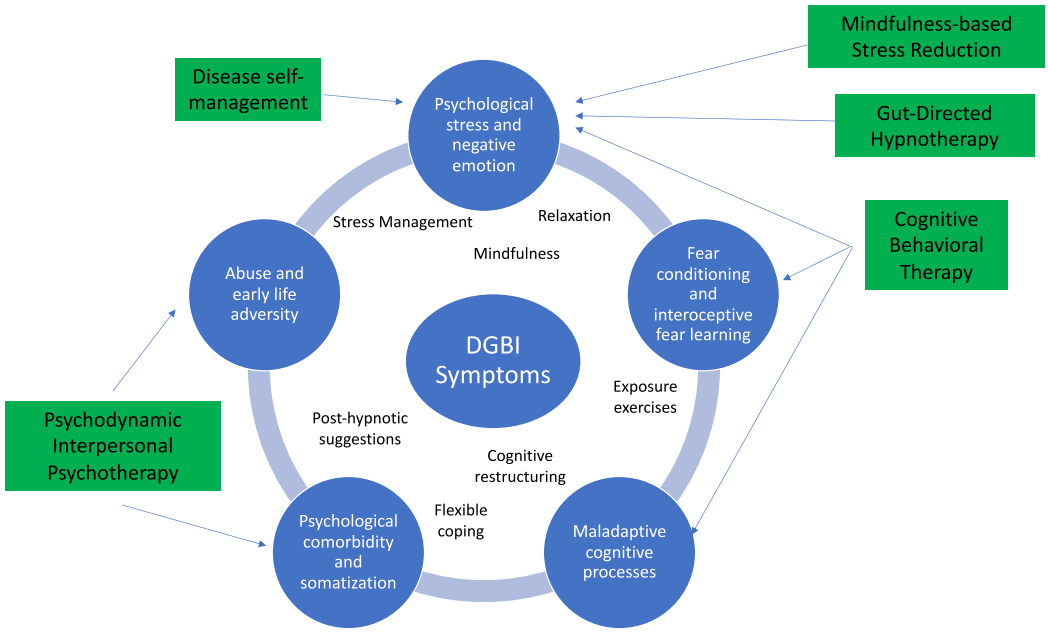

Figure 1. Brain-Gut behavior therapy targets and techniques by class.

aversive visceral signals to peripheral stress systems capable of affecting GI sensorimotor functions.

Another important link that is activated by stress is the hypothalamus-pituitary axis with its neuroendocrine mediators, including corticotropin-releasing hormone and cortisol.[54] While other mechanisms also exist, including systemic and local immune functions and the intestinal microbiota, which are increasingly acknowledged to play a role in DGBI,[55,56] the autonomic and stress hormone mechanisms are most easily appreciable by patients, consistent with broad evidence of altered autonomic nervous system functioning and stress hormone responses in DGBIs and other health conditions associated with chronic stress, and clearly modifiable by most classes of BGBT.

There are several ways in which the central or peripheral pathways of the gut-brain axis can become dysregulated. Stress is one of the most prominent and well characterized psychological factors, affecting DGBIs by modulation of visceral sensorimotor functions. Learning is another, less widely appreciated, example, which like stress often constitutes a primary therapeutic target in most classes of BGBT. The next section highlights some of those modifiable targets.

Clinical Connection:
We have previously recommended that providers master patient-friendly language on the gut-brain axis to reduce stigma and engage skeptical patients in the rationale for BGBTs for their seemingly "medical" disorder.[3,57,58] For more information on patient-friendly ways to explain the gut-brain axis, see Drossman DA, Ruddy J. Gut feelings: disorders of gut-brain interaction and patient-doctor relationship. Chapel Hill, Drossman Care, 2021 (video: https://romedross.video/DrossmanBrainGut).

Section III. Targets of BGBTs

In this section, we review the common brain-based and behavioral contributors to gut-brain dysregulation, and set the stage for how certain BGBT techniques might be applied based on the patient's unique presentation (Figure 1).

Fear Conditioning and the Development of Visceral Hypersensitivity and Hypervigilance

Patients can usually recognize that they have become afraid of having GI symptoms because of their unpleasant, unpredictable, and embarrassing nature. They may also be able to give examples of situations (eg, eating, going for a long walk, riding the subway) that they avoid because of fear. Discussing fear conditioning as part of gut-brain dysregulation can often be quite helpful in convincing patients to pursue BGBT, particularly exposure-based CBT.[59,60]

Laboratory studies have underscored that prior experience and learning processes, comprising classical conditioning, instrumental learning, and social observation, shape and interact with treatment expectations within any given clinical or experimental context.[61] Conditioning studies in DGBI focus on the role of learned fear in response to gut sensations.[62,63] Because patients with DGBI are characterized by hypervigilance, excessive symptom-specific fear and distress,[64,65] and excessive avoidance behavior,[66] the strong associability of unpleasant and benign visceral sensations might be an ecologically valid target for future research relevant to the pathophysiology and treatment of chronic visceral GI pain. There is great potential arising from conditioning studies,[67] including the opportunity to elucidate the role of memory and learning, in line with a cognitive neurobiology of visceral pain in DGBI.[68]

The Impact of Psychological Stress and Negative Emotions on Symptom Perception

A subset of patients are able to identify stress and mood leading to a worsening of GI symptoms, or conversely to report that chronic GI symptoms lead to or worsen levels of chronic stress. This patient insight can be leveraged to explain the concept of the bidirectional gut-brain axis and why it is sensitive to stress, and can serve as a lead-in to explain how BGBT approaches these concerns.

Stress-related acute and chronic psychological states and traits affect pain perception and coping, which can in turn negatively affect overall psychological health and resilience as part of a vicious cycle. In addition to stressful life events in childhood and adulthood, which demonstrably increase DGBI risk (see below), chronic rather than acute stress is likely more relevant to DGBI onset and course. However, acute psychological states are also important modulators of visceral perception and GI functioning, and knowledge derived from well controlled experimental laboratory studies have been instrumental as a scientific basis for the gut-brain axis in general with relevance to specific BGBT techniques.

Briefly, experimental laboratory studies have assessed the effects of different types of acute stressors, specific negative emotional states, and neuroendocrine stress mediators in the context of visceral sensorimotor functions in healthy individuals as well as in patients with DGBIs.[69,70] Collectively, these studies document that visceral perception is modulated by acute stress and negative emotions—in other words, that stress and negative emotion amplify gut sensations and drive symptom reporting. In IBS, brain imaging data support that acute stress or experimentally induced negative mood alters neural activation in response to aversive visceral stimuli, involving multiple brain regions, including the insula, cingulate cortex, and prefrontal areas. Such modulation has been demonstrated in healthy individuals,[71] but appears to be more pronounced in DGBI patients,[72,73] Lower resilience to stress in IBS is also reportedly associated with GI symptoms and altered cortisol responses in IBS[74] and may be improved with gut-directed hypnotherapy.[75] Thus, while patient conceptualization regarding the role of stress may focus more on chronic stress, it can be helpful to increase motivation for specific BGBT techniques to explain the impact (and therefore the potential) of making small changes in acutely stressful situations. These have the potential to improve symptoms independently as well as reduce chronic stress and negative mood.

Stress and stress mediators also have impacts on conditioning effects, linking emotional and cognitive facets relevant to pathophysiology and treatment. Classically conditioned anticipatory responses to visceral pain are sensitive to cortisol levels in healthy individuals[76] and involve the corticotropin-releasing factor signaling system in IBS.[77] Furthermore, effects of negative expectations on visceral pain perception are reportedly enhanced by acute psychosocial stress.[78] Given broad evidence on the role of stress in learning and memory processes, this emerging concept provide links not only within, but also across, fields,[79] raising the question of whether stress contributes to the maladaptive catastrophizing cognitions and negative symptom reporting biases observed in IBS.[80]

Abuse, Early Life Adversity, and Post-traumatic Stress

Abuse history can amplify the illness experience and clinical behaviors. This subset of DGBI patients are often high health care utilizers, and they may be challenging to clinicians who feel limited in their ability to understand and care for them. Clinicians need to be prepared to identify when this history is clinically relevant and to refer if needed.

In keeping with the role of chronic stress in DGBIs, it has been well established in a large national population study that adverse childhood experiences, including childhood sexual, physical, and emotional abuse, neglect, and household dysfunction, particularly mental illness or incarceration of a parent, result in a 2-fold increase in the risk of developing IBS.[81] We also know that the compounding of adverse experiences can increase the odds of developing IBS[82] and that IBS patients report more adverse life events than healthy control subjects.[83] Drossman et al[84,85] has reported that up to 50% of women seen in academic gastroenterology practices report a history of early trauma, and this history is associated with more significant pain reports and poorer health outcomes.[86]

Several clinical features may point to the possibility that a patient has experienced sexual, physical, or emotional trauma.[84] GI disorders commonly associated with abuse history include chronic abdominal and pelvic pain, constipation with dyssynergic defecation, morbid obesity, eating disorders, and multiple DGBIs and functional somatic syndromes. Comorbid psychiatric disorders may include severe anxiety and depression, post-traumatic stress disorders, panic disorders, stress-related disorders, dissociative somatic symptoms, sexual dysfunction, and personality disorders.[87] Behavioral features include frequent use of health care services, strong denial of the role of psychological factors influencing symptoms, a history of multiple diagnostic procedures, treatments, and surgeries, and anxiety related to endoscopic rectal or pelvic examinations.

Finally, early-life adverse events have been shown to cause persistent corticotropin-releasing factor systems and dysregulation of the hypothalamus-pituitary axis, resulting in heightened stress response, which may explain the link between DGBIs and trauma more broadly.[86] Post-traumatic stress has been associated with an increased likelihood of IBS.[87] It is beyond the scope of this WTR, but the neurobiology of PTSD and IBS is an important area of future study.

Clinical Connection:
For more information on approaching abuse history with patients, see Drossman DA. Abuse, trauma and GI illness: is there a link? Am J Gastroenterol 2011;106:15–25 (video: https://romedross.video/Medscape1015Trauma).

Maladaptive Cognitive Processes Can Affect Central Processing, or the Interpretation, of Gut Sensations

In the way a patient describes their GI symptoms (eg, "I just know if eat *x* I will have a problem"; "I cannot handle this anymore—you have to do something!"), clinicians are often able to identify evidence of maladaptive cognitive processes that may be amplifying symptom experience and reducing quality of life.

The development of maladaptive cognitions around GI symptoms is common and likely related to learned experiences and expectations. For example, visceral anxiety, or worry about the potential occurrence of symptoms and the potential for them to occur in certain settings, can become reinforced by beliefs that avoiding these unpleasant situations is preventive.[66] The worry about symptoms increases the likelihood that they will be over-identified and experienced as more threatening.[88,89] Similarly, catastrophizing, the belief that the GI symptom is dangerous and the belief that one is helpless, or ill equipped to cope, has been shown to prohibit down-regulation of gut sensations in addition to activating emotional centers of the brain at the point of GI sensory input.[73] Similarly, underlying processes (core beliefs) driving these cognitions may include themes of rigidity or psychological inflexibility,[90] perfectionism, overresponsibility, and approval-seeking which may also affect symptom experience.[91]

Psychological Comorbidity and Somatization Can Affect Symptom Experience

Psychological comorbidity and somatic syndromes are present in approximately 40% of DGBI patients, and patients are often relieved to hear that this may be a response to DGBI symptoms and inadequate coping.

Indeed, a large proportion of DGBI patients experience psychological comorbidities, most notably anxiety and depression, and report bodily symptoms originating both from inside and outside the GI tract, including symptoms of fibromyalgia, chronic fatigue syndrome, overactive bladder, chronic pelvic pain, and other chronic pain syndromes.[92] This large and relatively non-specific spectrum of comorbidity is consistent with the broad role of sensitization of the gut-brain axis and is highly relevant to behavioral treatment approaches where psychosocial and biological factors play a role in the transition from acute to chronic symptoms as well as in maintaining symptom chronicity.[73] Comorbid post-traumatic stress disorder may also influence the perception of DGBI symptoms, in part owing to its association with chronic hyperarousal, exaggerated stress response, and hypervigilance; mindfulness interventions may target this pathway in comorbid PTSD and IBS.[93]

In DGBI, comorbid anxiety, depression, and chronic stress correlate with the severity of GI symptoms, contribute to altered structural and functional brain measures, and negatively affect quality of life and health behaviors, such as increased health care seeking and poor adherence.[73,94,95] Several prospective studies support that symptoms of anxiety and/or depression can precede the first manifestation of a GI diagnosis, supporting their role as risk or vulnerability factors.[96] At the same time, the prospective risk for new-onset symptoms of anxiety and depression is increased by chronic GI symptoms. In other words, the GI condition precedes and is associated with the de novo development of psychological disorders.[96]

Clearly, there are several modifiable brain-tgut targets that could respond to behavioral intervention. Advances in neuroscience and behavioral intervention science have allowed for an evaluation of individual BGBT techniques, allowing for improved treatment decision making among BGBT providers and those referring. The reader will notice that many techniques cut across classes of BGBT. Many of the most common techniques are offered by medical providers, nurse or nurse educators, and mid-level mental health providers, whereas some of the more unique or specialized techniques are more suited to doctoral level therapists (gastrointestinal psychologists).

Section IV. Common and Unique Therapeutic Techniques Seen in BGBT

In this section, we have broken down the core elements of BGBT into common or universal techniques, meaning they are present in nearly all classes of BGBT, and then into specific or unique techniques that fit within the class of BGBT and/or the mental health provider's conceptualization of the patient's specific case.

Common/Universal Techniques in BGBT

Strong patient-provider relationship. At the heart of any treatment for DGBIs is the patient-provider relationship. An effective relationship can enhance diagnostic accuracy and clinical decision making by obtaining more meaningful information, improve the time efficiency of a visit, improve patient and provider satisfaction, and reduce patient requests for more tests or health care services.[57,97] There are challenges to fostering this relationship that are beyond the scope of this WTR but are nicely presented in a previous WTR.[98] Doctors need to see more patients in less time and handle more administrative duties, shifting the focus away from the patient. They receive less reimbursement from third-party payers, and turn to tests as a seemingly time-efficient way to make a diagnosis. Unfortunately in DGBIs, tests get to the structural or biological abnormalities, not the patient's thoughts and feelings about their illness. These changes result in a less satisfying experience for patient and the doctor. Doctors often report they are losing the connection to their patients; patients feel diminished with their role and often respond with frustration and, at times, self-blame and -stigmatization.[57] A strong patient-provider relationship is accomplished through using effective communication skills and is associated with increased patient satisfaction, adherence to treatment, and improved clinical outcomes, including symptoms reduction.[57] An effective patient-provider

relationship will permit recommendations such as referral to a therapist to be more accepted.

Clinical Resources:
For example scripts to communicate the brain-gut axis and the referral to BGBT, see Keefer L, et al. Best practice update: incorporating psychogastroenterology into management of digestive disorders. Gastroenterology 154;2018:1249–1257.
Educational resources to learn skills that enhance the patient-provider relationship are e available through the Rome Foundation (video: https://romedross.video/3blx535).
For an in-depth look at the patient-provider relationship from the physician and patient perspectives, see Drossman DA Ruddy J. Gut feelings: disorders of gut-brain interaction and patient-doctor relationship. Chapel Hill: Drossman Care, 2021.

Psychoeducation. Patient education includes both transfer of knowledge and support for self-management, by which the patient can develop an ability to understand and manage symptoms in daily life.[99] It is especially important to identify and address the patient's thoughts, fears, and pre-conceptions about their diagnosis,[100] decrease stigma, and instill hope for change. Providing reassurance that IBS does not increase the risk of serious medical conditions (eg, cancer) is also critical. Other significant educational opportunities in DGBIs include patient-friendly explanations of DGBI pathophysiology, the gut-brain axis, the diagnostic process, including a positive diagnosis of a DGBI, the natural fluctuation of symptoms, and the role of diet, physical activity, sleep, and stress on the gut. Psychoeducation can help the patient to recognize the role of the gut-brain axis and psychological factors in their own symptom experience[101] and motivate them for BGBT. Information about DGBI treatment options that are available and how they work is important, as well as explaining that a combination of treatment modalities (eg, pharmacologic, dietary, and psychological) is common, and not a "last ditch" effort. Realistic expectations of symptom improvement are important and have to be defined in the treatment plan and clearly shared with the patient.

Stress management. Stress management is an umbrella term for interventions that aim to improve skills that can be used to effectively reduce or prevent acute and chronic stress, given the impact of stress on symptom and symptom perception. Stress management leverages different skills and approaches, many of which are included below, based on which aspects of stress (eg, emotional/cognitive, autonomic, neuroendocrine) are being targeted. A typical stress management intervention will begin with helping the patient to identify the stress-symptom relationship and triggers of stress and symptoms, often using self-monitoring stress and symptom diaries. Psychoeducation about lifestyle changes that can reduce stress, including problem-solving, relaxation techniques,[102] sleep hygiene, and social support, are often combined with other specific techniques, depending on the skill and training of the provider implementing the program.

Relaxation training. Modification of hyperarousal is a core component of most BGBTs because of the stress-sensitive nature of DGBIs. There are several different approaches to relaxation training, and this is often decided based on patient preference because evidence for one technique over another is not established. Relaxation skills can be used in real time to manage bothersome symptoms or be incorporated as part of a general stress management routine focused on reducing baseline levels of arousal. Commonly used relaxation techniques include progressive muscle relaxation, relaxation response meditation, autogenic training, guided imagery, and diaphragmatic breathing. In most cases, relaxation training is taught by the provider to the patient in a session, demonstrating a relaxed physical position, quieting the mind and body in a space free from distractions or interruptions, and is then practiced at home between sessions. For example, autogenic training, a standardized relaxation technique[103] that can be taught to the patient for home practice by physicians and allied health providers, is widely used for psychosomatic conditions[104] and has shown some evidence of effectiveness in IBS.[105] See Shah et al[106] for an excellent overview of relaxation training in IBS.

Diaphragmatic breathing. Relaxation and diaphragmatic breathing help to increase vagal tone, which is altered in DGBIs. Diaphragmatic breathing is often used as a stand-alone self-regulatory intervention for rumination disorder owing to its association with improved gastric accommodation and normalizing the pressure gradient at the lower esophageal sphincter. It has also been used successfully in abdominophrenic dyssynergia when patients have visible abdominal distension.[107] In this technique, the patient is taught to engage in the breathing exercises in advance of a meal, during/half-way through a meal, immediately after a meal, and 30 minutes after (or 90 minutes if patient has delayed symptoms). Although data for diaphragmatic breathing in rumination is strongest,[108,109] this approach is used for a variety of meal-related symptoms, including dyspepsia, fullness, and fear of eating. Diaphragmatic breathing can also be used as a competing behavior for excessive or supragastric belching and can be part of a breathing retraining program for aerophagia. For a video demonstrating the technique, see https://www.youtube.com/watch?v=UB3tSaiEbNY.

Advanced/Specific BGBT Techniques

Post-hypnotic suggestions. The key ingredient for success in gut-directed hypnotherapy is the language used around the person's unique DGBI symptoms. Therapists are trained both in basic aspects of inducing a hypnotic state and in the development of metaphors or "scripts" that apply directly to their patient's concern. After patients are put into a highly relaxed and focused state through both instructions on muscle relaxation and pleasant imagery, the trained therapist will deliver post-hypnotic suggestions (the key therapeutic ingredient). Common themes across several protocols (eg, Manchester Protocol,[110] North Carolina Protocol[111]) include suggestions of increased comfort, reduced

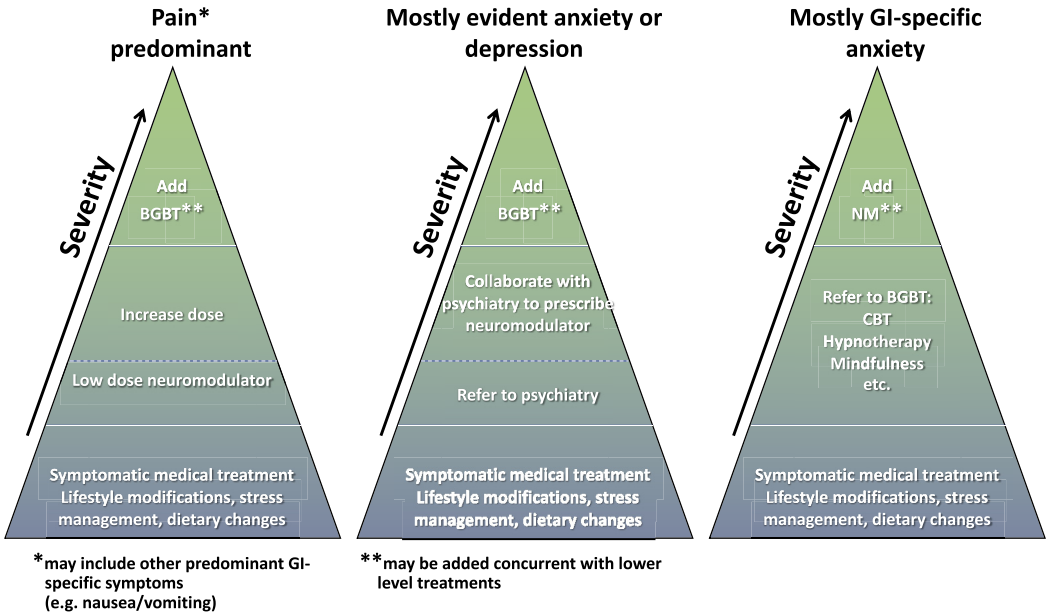

Figure 2. Approach to integrating BGBT into the care of disorders of gut-brain interaction. BGBT, brain-gut behavior therapy; CBT, cognitive behavioral therapy; GI, gastrointestinal; NM, central neuromodulator.

attention to sensations, feelings of warmth or cooling, and the body restoring back to its natural state.

Mindfulness. Mindfulness is a meditation practice inspired by Buddhism where one carefully observes one's stream of conscious experiences, eg, perceptions, thoughts, feelings, and sensations, without judging these experiences as good or bad or true or false.[112] Importantly, although mindfulness practices may invoke feelings of relaxation, they are not considered relaxation exercises and are instead conceptualized as strategies to reduce vulnerability to stress. Mindfulness for DGBIs focuses on reducing overall arousal and stress and decreasing the risk of symptom flare-ups.[39] More specifically, mindfulness aims to regulate patients' negative emotional and cognitive reactions to their GI symptoms,[38] which can exacerbate symptoms. A formal mindfulness protocol (mindfulness-based stress reduction) includes 8 weekly 90–120-minute training sessions and daily mindfulness exercises that patients do at home.[39] Many patients and clinicians use mindfulness-based exercises as an adjunct to CBT or as part of other contextual behavioral therapies, such as acceptance and commitment therapy.[24]

Interoceptive and in vivo exposure and behavioral experiments. Adding exposure to CBT may be particularly important for patients with moderate to high levels of avoidance behavior.[113] Fear of GI symptoms, a learned behavior, can include fear of incontinence, sense of not being able to function because of pain, and discomfort because of constipation or bloating. Exposure therapy is defined as a repeated approach to stimuli that elicit fear (or other learned aversive emotions), without attempts to control the stimuli or the elicited emotion, to reduce the

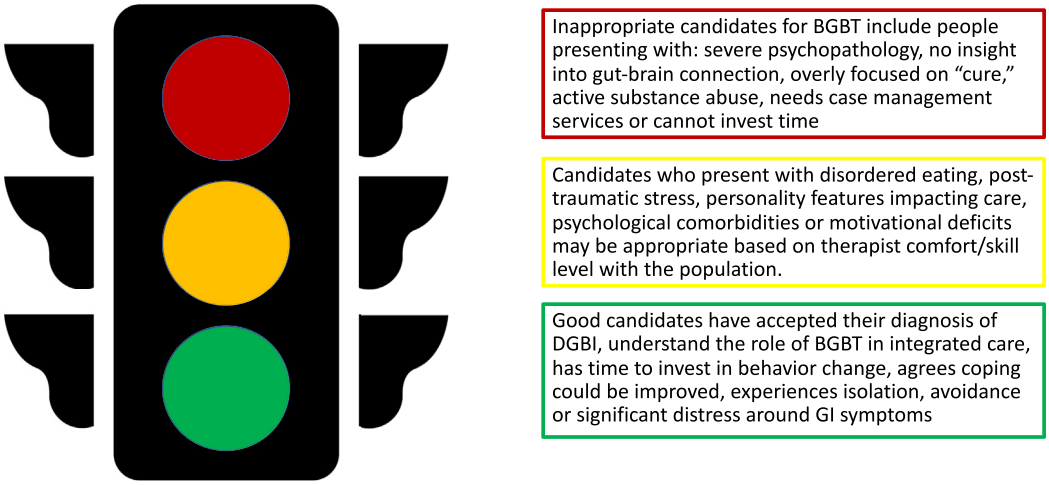

Figure 3. Choosing the right candidate for BGBT. BGBT, brain-gut behavior therapy; CBT, cognitive behavioral therapy; DGBI, disorder of gut-brain interaction; GI, gastrointestinal.

Table 2. Resources for Accessing Behavior Therapists in the Community

Resource	Website
Rome Foundation GastroPsych Clinician Directory	https://romegipsych.org
Psychology Today Therapist Finder	www.psychologytoday.com/us/therapists
American Psychological Association	https://locator.apa.org
National Register of Health Service Psychologists	https://www.findapsychologist.org
Association for Behavioral and Cognitive Therapies	http://www.findcbt.org

When searching the above websites for therapists, you do not necessarily need to find a gastrointestinal psychologist. Look for specializations in chronic illness or chronic pain, because those therapists often have training in health psychology and working within a medical team. You can also look for therapists who report that they provide some of the evidence-based behavior therapies such as cognitive behavioral therapy or hypnotherapy, because these too can often be adapted for disorders of gut-brain interaction by a well trained therapist. Finally, if you find a therapist in your community who is interested in working with patients with disorders of gut-brain interaction, they can participate in continuing education programs through the Rome GastroPsych group at www.romegipsych.org.

fear of the stimuli—in other words, unlearning the fear conditioning.[59] In interoceptive exposure, patients with DGBIs will expose themselves to visceral sensations, for example, by eating foods that trigger symptoms, physical exercise, wearing tight clothes, or delaying and reducing bathroom visits.[59,114] In vivo exposure for DGBI entails engaging in situations where symptoms are unwanted, for example, being far away from a toilet, sexual activity, or going to dinner.[59,114] Exposure exercises may also be framed as behavioral experiments that are designed to test specific hypotheses that the patient has about the outcome of a specific behavior in a specific situation.[115] For example, a patient could test their prediction that they are unable to perform at work if they are in pain by recording the number of work tasks that they actually accomplish during a work day when they feel abdominal pain. The goal of exposure exercises is to experience that the feared outcome, for example, not being able to cope with painful symptoms, does not occur, which leads to new learning that the situations are less dangerous than previously perceived. Importantly, patients need to abstain from "safety behaviors" that serve to reduce the perceived threat of the situation (eg, bringing extra underwear when riding the bus).

Cognitive restructuring. Cognitive restructuring is one of the most commonly advanced CBT techniques, is taught by a trained provider, and is based on the premise that emotions stem from our interpretation of events, not the events themselves. The goal of restructuring is to identify thoughts that may be unhelpful or maladaptive and to restructure, or re-evaluate, them in a way that is either more accurate, more accepting, or more helpful. For example, a patient may be asked to re-evaluate the probability of an event actually occurring based on prior experience rather than future worry (how many times have you actually not made it to a bathroom?). They might be asked to answer their worry as if they were talking to a friend instead of themselves. They might be asked if their belief would hold up in a court of law. Common maladaptive thinking patterns that are targeted in DGBIs include pain catastrophizing and visceral anxiety/probability overestimation. To teach cognitive restructuring, therapists may assign thought worksheets for completion between sessions to facilitate real-world skill acquisition.

Flexible coping training. There are data suggesting that patients with DGBIs, including IBS and functional dyspepsia, have some difficulty effectively choosing between problem-focused coping and emotion-focused coping[90] in the setting of a problem or concern. The most common concern is patients failing to apply emotionally focused coping techniques (acceptance, seeking support, relaxation, self-care, prayer) to an unsolvable situation. In flexible coping training, therapists help patients reframe problems into smaller pieces, determining which aspects are controllable by the patient and which aspects are not, and then help them choose their coping strategy based on controllability (problem-focused for controllable, emotion-focused for uncontrollable).

Knowing the science behind BGBTs as well as their associated targets and common and specific techniques is a critical first step to the successful integration of BGBT into clinical practice.[3] See Figure 2 for examples of ways in which BGBT can be incorporated into GI care based on a patient's presenting concern. The final section of this paper focuses on who to refer and how to refer in a way that increases uptake.

Section V. Who and How to Refer for BGBT

In general, any patient with a DGBI who notices a relationship between stress and symptoms, who is reporting difficulty coping with symptoms or other health-related factors, who reports or exhibits maladaptive behaviors in response to their symptoms, or who is interested in the mind-body or gut-brain connection, is a good fit for BGBT (Figure 3).

Table 3. Future Research Needs

- Prospective studies to identify what psychological or clinical characteristics predict treatment response (→ personalized selection of BGBT)
- Research addressing the combination of pharmacotherapy and other types of non-behavioral interventions (eg, diet) and BGBT
- Mechanistic studies on gut microbiota and visceral hypersensitivity and psychological comorbidities
- Well designed studies that identify the most effective classes and/or techniques, potentially matched to patient characteristics

BGBT, brain-gut behavior therapy.

There may be some instances in which it is unclear whether a patient is appropriate for a BGBT referral or whether a referral to a general mental health practice is needed. Mental health comorbidities are common in DGBIs, and it is important to understand which of these require targeted psychiatric treatment outside of the psychogastroenterology setting. In general, patients in need of treatment for obsessive compulsive disorder, eating disorders, substance abuse, psychosis, severe depression or anxiety, and personality disorders need to be referred to a provider with specialization in those areas. Once treatment for these comorbidities is established, it is often appropriate to also refer for BGBT consultation. Indeed, many patients receiving BGBT treatment are also followed for long-term therapy in the community. Utilization of specific health psychology billing codes allows for insurance coverage of these concomitant treatments.

How to Refer

Once a medical provider has determined that a BGBT referral is appropriate, the next step is to discuss the referral with the patient. Ideally, medical providers will have already introduced this service to all patients as part of integrated care, established an effective relationship, and provided psychoeducation. When this has been done, a referral to BGBT can be presented and understood as a logical step in the management of their condition. Even if this foundation has not been established, however, there are ways to present a BGBT referral that can encourage openness and success with treatment. For example, it is very important that a referring provider master patient-friendly language to describe the role of the brain-gut pathway in DGBIs and be comfortable discussing the perpetuating and maintaining factors of GI symptoms.[3] This will vary based on the provider's personal style, and we encourage all providers to consider and even practice different ways of discussing this referral. For an example dialogue, see the video at https://romedross.video/KeeferTherapy.

What to Expect After a Referral

For a patient to experience the full benefits of BGBT, it is important that their medical provider and therapist communicate about treatment goals and progress. When a BGBT provider is embedded in a medical practice, this can happen naturally through electronic medical records, e-mail, and in-person consultation. In this model, it is important that the BGBT provider communicate to the patient that they are part of the patient's medical team and that information about treatment progress and goals will be shared with the physician. When the BGBT provider is not affiliated with the clinical practice, however, there are several proactive steps that can be taken to facilitate this communication. First, the medical provider can discuss with the patient the benefits of direct communication between the physician and the therapist. If the patient agrees, the physician can proactively provide a HIPAA (Health Insurance Portability and Accountability Act) release form for the patient to present to the BGBT provider at their initial visit. For more information on HIPAA privacy please consult the US Department of Health and Human Services website: https://www.hhs.gov/hipaa/index.html.

For resources and strategies to find a qualified therapist in your community, see Table 2.

Conclusion

It is our working team's strong recommendation that BGBT be incorporated as part of integrated care in DGBIs. Although many patients may be readily managed by the GI provider as part of traditional clinical practice, we recommend that the threshold for a referral to BGBT be lowered; this recommendation is based on robust science supporting a mechanistic link to the brain-gut axis, the working team's literature review, and expert consensus around the specific targets of BGBTs and evaluation of the common and unique techniques associated with each successful class of BGBT, many of which are more similar to each other than different. Both GI providers and gastropsychology clinicians have an opportunity to optimize care for DGBIs through a collaborative integrated approach that begins with an effective patient-provider relationship, thoughtful communication about the brain-gut axis and, when appropriate, a well communicated referral to BGBT. Directions for future research are recommended in Table 3.

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Conflicts of interest
Laurie Keefer reports consultancy to Abbvie, Pfizer, and Reckitt Health, cofounder and equity owner of Trellus Health. Brjánn Ljótsson reports shares in DahliaQomit, a company specializing in online psychiatric symptom assessment, and Hedman-Lagerlöf och Ljótsson Psykologi, a company that licenses cognitive behavior therapy manuals. The other authors declare no conflicts.