ADVANCES IN IBS

Current Developments in the Treatment of Irritable Bowel Syndrome

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The Promise of Digital Therapeutics for Disorders of Gut-Brain Interaction

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G&H Why is it important to address unhealthy behavior patterns in patients with disorders of gut-brain interaction? What are the main targets for intervention?

KS Typically, disorders of gut-brain interaction (DGBI), with irritable bowel syndrome (IBS) being the prototype, can be thought of in 3 different ways. First, there is abnormal signaling in the nerves in the gut sending abnormal signals up to the brain through pathways that may be upregulated; second, the brain is receiving that data, which may be faulty, and interpreting that data; and third, the brain potentially sends signals back down to the gut that can affect how the gut works. Unlike most DGBI medications, which principally target peripheral mechanisms of motility and sensation, brain-gut behavioral therapies (BGBTs) instead focus on how abnormal signals from the gut are interpreted by the brain. Focusing on this often-neglected DGBI mechanism provides patients with the tools to recognize these signals as abnormal and change the way the body responds—resulting in a meaningful improvement for many patients. Cognitive behavioral therapy (CBT) and gut-directed hypnotherapy are the 2 most evidence-based BGBTs. Both have the ability to alter dysregulation of the brain-gut axis, which may include reducing arousal related to abnormal gut perception and improving coping mechanisms as a palliative strategy. However, a variety of different BGBTs are available, and all are, at their core, about changing the response to abnormal signals arising from the gut in patients with DGBI.

G&H Who is the ideal candidate for BGBT? Are there patients in whom this therapy might be contraindicated?

KS Behavioral therapies tend to be thought of as treatment for patients with psychiatric disorders, when in reality patients with moderate to severe psychiatric symptoms often need a carefully constructed behavioral health team with individualized therapy plans. BGBTs are better for patients who have either no psychiatric disorder or very mild psychiatric symptoms and no concurrent disordered eating or substance abuse. It is also important to identify a patient who is accepting of this type of treatment (meaning someone who is not necessarily looking for an instant fix), can recognize the role of stress and other factors in modulating their DGBI symptoms, and is open to the idea of the brain-gut connection as driving at least some of their symptoms. Although many patients will recognize this pathway as relevant and important, not every patient will feel the same way or be open to the concept. Finally, candidates for BGBT need to be motivated to do their homework.

G&H What are the challenges with providing BGBT to patients as a component of integrated gastrointestinal care?

KS For a while, BGBTs were on the periphery and not necessarily accepted as standard of care. However, gastroenterology providers now understand that BGBTs are not only effective but also complementary to some of the traditional medical therapies already in place. Fortunately, the stigma surrounding these types of therapies is slowly breaking down as well, meaning more acceptance by both patient and provider. Yet, the biggest problem may be access. CBT and gut-directed hypnotherapy require a clinician with specific training, typically a gastrointestinal (GI) psychologist. There is currently a limited supply of providers who offer these therapies to patients. In a city like Boston, where I practice, we are fortunate to have these providers as part of our care team, yet wait times to see them are still unacceptably long. Such lack of access is a significant barrier to the adoption of CBT and gut-directed hypnotherapy: how can we connect patients to these effective therapies when access is such an issue? Another barrier is payment models. Reimbursement can be variable, so finding a sustainable care model that keeps patients, providers, and payers happy remains a significant challenge.

G&H What are digital therapeutics, what are they designed to do, and how could they help patients with DGBI?

KS Digital therapeutics (DTx) can encompass a wide variety of interventions. The most well-known of the DTx are apps that provide an intervention meant to diagnose, treat, or monitor a medical condition—in this case, a DGBI. Apps often come in the form of connected devices such as wearables that may monitor an aspect of our physiology (eg, heart rate, sleep, activity), which many people already wear every day, or symptom trackers that allow users to keep a diary of symptoms to enhance understanding of their illness. Of the DTx available, apps are the predominant focus of BGBTs. An advantage of DTx apps is that they can help democratize the BGBT field. Right now, the vast majority of patients do not have access to a GI psychologist or BGBTs. It is hoped that apps can step in and fill this role, connecting more patients to treatments that would otherwise be unavailable owing to limited therapist availability, geographic constraints, or financial barriers. Although an app may not be equivalent to having personalized recommendations from an expert in the field, it is important, in my opinion, to not let perfection be the enemy of good. On the whole, apps can bring BGBTs to more patients who would never have the opportunity to benefit from these treatments otherwise.

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G&H Which of the evidence-based BGBTs can effectively be delivered by DTx?

KS The 2 most studied BGBTs using DTx are CBT and gut-directed hypnotherapy. Although the evidence for these BGBTs is robust, it is difficult to generate the same type of evidence seen for pharmacotherapies. However, there is a US Food and Drug Administration (FDA) clearance pathway for DTx that provide BGBTs, allowing manufacturers the opportunity to make claims about both safety and efficacy. The landscape of products offering either gut-directed hypnotherapy or CBT is changing very rapidly. The only 2 mobile apps that were cleared through the FDA pathway, Mahana IBS (Mahana Therapeutics), a gut-directed CBT for IBS, and Regulora (metaMe Health), a gut-directed hypnotherapy, cannot be prescribed in the United States right now, despite being in existence for some time. Implementation barriers, including reimbursement, have likely played a role in the exit of these early DTx innovators from the US market. Of course, there are other non–FDA-cleared apps that provide gut-directed hypnotherapy and CBT with some efficacy and safety evidence suggesting their utility—but without the reassurance of FDA clearance to help consumers who may not be as familiar with the literature.

G&H Which of the currently available apps that provide virtual behavioral health interventions for patients with IBS do you recommend?

KS Right now, Nerva (Mindset Health) is one of the few apps that has some evidence of efficacy and is still available. It offers a 6-week mobile app–delivered gut-directed therapy program distributed over 42 sessions during which patients receive gut-directed hypnotherapy recordings that are meant to be practiced daily. Because it does not require a prescription, I have found that many patients who would naturally gravitate toward nonpharmacologic approaches and have self-identified the role of the brain-gut connection in their symptoms may have discovered and completed Nerva on their own. Still, other patients are open to this pathway after I explain it to them

in the office and subsequently become enthusiastic users. However, for some patients, Nerva does not generate the level of engagement needed and thus is less effective.

G&H What behavioral health DTx are in development?

KS Future DTx will likely continue to offer BGBTs such as CBT and gut-directed hypnotherapy in both traditional and new, innovative forms. As mentioned, DTx are beginning to integrate physiologic measurements. Already available is a breath-testing device that can be used after each meal to measure the level of fermentation for particular foods and correlate it to symptom severity over time via an integrated app. The information collected in the app can help patients determine, potentially, what specific foods they may be more sensitive to vs others. There are also apps providing cross-platform integration (ie, apps that are able to track symptoms and offer BGBTs as well as measure physiologic outcomes) that may help add some evidence base for changes in disease management. Many behavioral health apps, especially the symptom-tracking apps, provide so much data for patients that it can be difficult for both the patient and the provider to sort out what is important. App developers are looking at how to organize data efficiently so that a busy clinician can quickly understand the implications for the patient.

> DTx will be most successful for patients with DGBI who practice any of the techniques outside the confines of their time specifically engaged with an app.

G&H How strong is the evidence for DTx?

KS If we extrapolate the data from studies of BGBTs, the evidence is quite strong. Looking at BGBTs administered in a digital fashion, the evidence is less robust but that is rapidly changing. A landmark study showed that digital application of gut-directed hypnotherapy was more effective than more minimal-contact therapy that also had some components of CBT. There is also emerging evidence showing that DTx are doing what they claim to do, as long as they are based on therapies with a good evidence base (ie, CBT and gut-directed hypnotherapy).

G&H What should be considered before recommending DTx to a patient?

KS The patient has to be an active participant. This is not a passive type of treatment. Generally speaking, the patients most likely to benefit from BGBTs are also likely to benefit from the current generation of DTx interventions. DTx will be most successful for patients with DGBI who practice any of the techniques outside the confines of their time specifically engaged with an app. Attrition with DTx is a significant concern. In a study on the real-world use of the Mahana IBS mobile app, which offers gut-directed CBT, my colleagues and I found that of 843 patients who started a digital prescription, only 38% completed half of the sessions. This attrition rate is similar to that for gut-directed hypnotherapy. Clearly, not every patient is appropriate for DTx via an app. However, patients who completed 5 of the 10 sessions offered in the app did derive a significant benefit, as measured by a reduction in the IBS Symptom Severity Scale score. One predictor of completion included older age, which is in line with other studies on adherence but also indicates that adoption of digital technology by older adults is increasing, perhaps out of necessity from living in an app-pervasive world.

G&H Are there any limitations to DTx?

KS One of the biggest limitations is the constantly changing landscape of DTx. Providers may grow comfortable with discussing the benefits and practicalities of a given digital therapy only for it to become unavailable a short time later. The same could be said for pharmacotherapy, but in reality the turnover from digital debut to out of business can be remarkably fast. Also, it may be difficult for providers to evaluate the evidence for DTx apps objectively. There needs to be a better way to amalgamate the data to show what each app does and its level of evidence that is comparable across apps. Another barrier that has made it difficult for DTx apps to thrive is the inability to find a good pathway for reimbursement. The FDA-cleared apps, for example, had struggled to obtain insurance reimbursement and were forced to shift the cost burden to the consumer, who may be unwilling to pay for the app. The challenge for app companies is to find a workable reimbursement method to be able to sustain their operations—to turn a profit and continue to offer their services to patients. The ideal way for an

app to monetize DTx is still unclear. One solution may be to incorporate the app into the integrated care model, which is more stable and can offer a variety of DTx in one location. An example is Oshi Health, which partners with health plans and employers to provide an integrated, virtual platform for GI care, including GI psychologists, registered dietitians, and GI providers. App companies could avoid the issue of insurance coverage and rely on self-pay, an approach that may be more stable over time.

G&H Do you see DTx as a replacement of or adjunct to a live GI psychologist?

KS DTx are an adjunct to, not a replacement of, a GI psychologist. Currently, access to GI psychologists in the United States is limited. For patients with mild or moderate symptoms, DTx can be helpful because they can increase access and can potentially save the GI psychologists for patients who need a more individualized treatment plan, or who have tried the apps but did not have improvement in their disease. DTx can be part of first-line treatment, as many patients will benefit. Patients who do not benefit can be more confidently referred to a GI psychologist.

G&H What should future research focus on?

KS The main research priorities involve the establishment of rigorous standards for evaluation of DTx that are very similar to those used with other interventions for DGBI, such as medications. Having a pathway where DTx can prove both their safety and efficacy will give providers (and payers) a good sense of which apps to recommend. As I mentioned, developers need to focus as a field on how to monetize the apps in a way that continues to allow widespread availability. The apps need to be priced fairly so that patients can afford them and the companies that build them can sustain their operations and continue their development. When a drug is approved by the FDA, it does not change; in contrast, apps can be constantly updated and can actually change based on user input, which is even more likely with emerging technologies such as artificial intelligence. The question is how to develop a regulatory pathway for apps that are part of a unique therapeutic space and will likely need continued assessment over time.

Disclosures

Dr Staller has served as a consultant to Anji, Ardelyx, Gemelli, GI Supply, Mahana, ReStalsis, Salix, Sanofi, and Takeda and has received research support from Ardelyx and ReStalsis.

Suggested Reading

Brenner DM, Ladewski AM, Kinsinger SW. Development and current state of digital therapeutics for irritable bowel syndrome. *Clin Gastroenterol Hepatol.* 2024;22(2):222-234.

Lackner JM, Jaccard J, Keefer L, et al. Improvement in gastrointestinal symptoms after cognitive behavior therapy for refractory irritable bowel syndrome. *Gastroenterology.* 2018;155(1):47-57.

Pathipati MP, Scott LL, Griser AC, Staller K. Real-world outcomes for a digital prescription mobile application for adults with irritable bowel syndrome. *Neurogastroenterol Motil.* 2024;36(7):e14811.

Saleh ZM, Chey WD, Berry SK. Behavioral health digital therapeutics for patients with irritable bowel syndrome: a primer for gastroenterologists. *Am J Gastroenterol.* 2023;118(8):1311-1313.

Varma S, Scott LL, Sibelli A, Pathipati M, Griser AC, Staller K. Digital gut-directed CBT may improve fecal incontinence in IBS. *Dig Dis Sci.* 2025;70(4):1441-1448.