

## CONFERENCE REPORT

## “The Gut-Brain Axis: How to Manage Pain Caused by This Cross-talk”: An Overview of the Symposium

“消化道-脑轴：如何管理这种交互作用引起的疼痛”：专题讨论会概述  
 "El eje estómago-cerebro: Cómo tratar el dolor causado por esta intercomunicación": Perspectiva general del simposio

Aditi Nerurkar, MD, MPH, *United States*

This conference report was provided by Aditi Nerurkar, MD, MPH, an integrative medicine physician at Harvard Medical School and the medical director of the Cheng-Tsui Integrated Health Center at Beth Israel Deaconess Medical Center, Boston, Massachusetts. She specializes in mind-body medicine, stress management, and lifestyle medicine. She is also a contributor to *The Atlantic* and *The Huffington Post*.

### BACKGROUND AND INTRODUCTION

Until recently, the basic assumption was that the enteric system and central nervous system functioned independently of each other with little communication. But emerging research suggests there exists a rich and dynamic interrelationship between these 2 seemingly disparate entities. Referred to as the gut-brain axis, this innovative construct offers us a new window into understanding the mind-body connection. In the context of gastrointestinal (GI) illness in particular, it may help to elucidate the complex mechanisms contributing to chronic pain in patients with functional GI disorders, organic GI disorders, and behavioral disorders that cause GI somatization.

The mechanistic features of the gut-brain axis are comprised of a complex set of interconnected pathways linking the enteric system to the nervous system (Figure). The brain receives a continual stream of afferent information from the gut, integrates this information with internal cues in the body and external signals from the environment, and sends a response back to specific target cells in the GI tract. This dialogue is imperceptible in most people, but in patients with GI illness, this communication can cause a host of negative sequelae, which may include the recurrent discomfort of irritable bowel syndrome (IBS), the psychological and behavioral disturbances leading to abdominal pain in anorexia nervosa, the intestinal inflammation in patients with Crohn's disease, autoimmune-mediated intestinal changes in those with celiac disease, and tissue degeneration from tumor formation in patients with GI malignancies. Yet irrespective of their variable initial etiologies, these downstream consequences often lead to significant physiological and psychosocial dysfunction, both of which can adversely impact a patient's quality of life. Historically, the management of these aforementioned consequences has focused mainly on treating the under-

lining disease, and to date, little has been done to understand why the gut-brain dialogue exists in the first place.

To help gain greater insight into the nature of this innate, bidirectional pathway of communication, the symposium “The Gut-Brain Axis: How to Manage Pain Caused by this Cross-talk” was held on May 4, 2015, in Salerno, Italy. Sponsored by the European Biomedical Research Institute of Salerno, the Medical Association of Salerno, and the Institute for Integrative Health, the symposium sought to elucidate how conventional and complementary medical systems currently understand this bidirectional cross-talk and how an integrative approach blending these 2 medical spheres might provide a new and innovative therapeutic perspective in the management of chronic pain in GI illness. The symposium featured 38 speakers from numerous academic institutions in 5 different countries (Table), and the symposium's presenters represented a wide range of medical specialties including gastroenterology, internal medicine, pediatrics, adolescent medicine, neurology, psychiatry, and integrative medicine.

### KEYNOTE PRESENTATIONS: ADDRESSING THE COMPLEXITIES IN UNDERSTANDING AND TREATING PAIN MODULATED BY THE GUT-BRAIN AXIS

The event began with 2 keynote presentations given by Drs Paolo Marchettini and Marco Lacerenza, respectively. These talks provided an initial framework for the symposium and introduced the audience to key terminology as well as broader concepts that were used throughout the event. The keynote addresses defined which structures comprise the gut-brain axis, classified the types of pain variants, and explained what constitutes the gut microbiome and metabolome and their impact on the gut-brain cross-talk. They also introduced larger, conceptual topics such as the biopsychosocial model of pain, the emotional implications for affected patients, and the impact of pain on the doctor-patient relationship. The keynote talks concluded with a phrase that was echoed throughout the symposium by the speakers who followed: *Pain is a complex condition with multifactorial inputs and therefore requires a complex and multifactorial approach in its management.*

After these initial keynote presentations, the symposium continued with a systems-based approach; there were 5 individual sessions, each with a disease-

#### Correspondence

Aditi Nerurkar, MD, MPH  
 anerurka@bidmc.harvard.edu

#### Citation

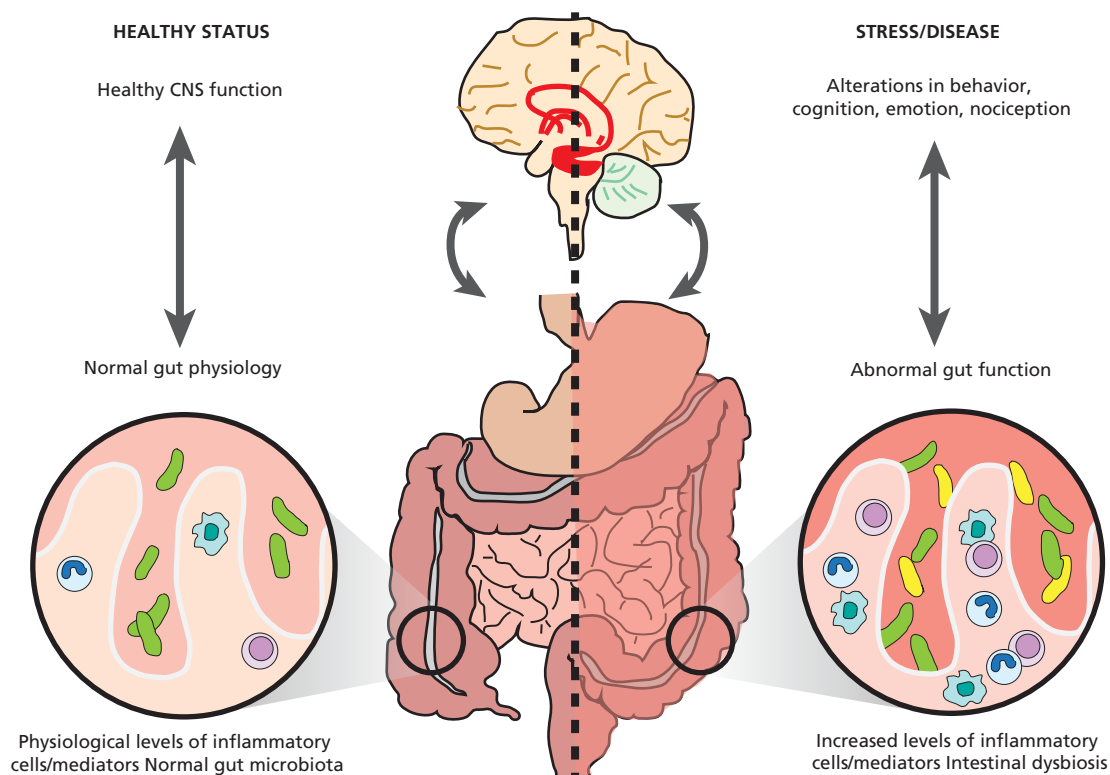
Global Adv Health Med. 2015;4(6):61-64. DOI: 10.7453/gahmj.2015.113

#### Key Words

Conference, gut-brain axis, disease, pain management

Table Symposium Attendees

Title	Speaker/Discussant	Institution	Medical Specialty
Professor	Paolo Barone	University of Salerno	Neurology
Doctor	Paolo Marchettini	Hospital San Raffaele, Milan	Neurology
Doctor	Marco Ruggero Lacerenza	Nursing Home S. Pio X; "Opera San Camillo" Foundation	Neurology
Associate professor	Rosario Cuomo	Federico II University Hospital School of Medicine	Gastroenterology
Doctor	Carlo Di Lorenzo	Nationwide Children's Hospital Columbus OH USA	Pediatrics
Professor	Justin Wu	The Institute of Digestive Disease The Chinese University of Hong Kong	Gastroenterology
Doctor	Francesco Cardini	Regional Health Agency of Emilia Romagna	Gynecology and obstetrics
Professor	Carmelina Loguercio	University of Naples	Gastroenterology
Professor	Alessio Maria Monteleone	University of Salerno	Psychiatry
Associate professor	Umberto Volpe	University of Naples	Psychiatry
Professor	Valdo Ricca	University hospital of Careggi, Florence	Psychiatry
Associate professor	Carlo Catassi	University Politecnica Marche	Pediatrics
Professor	Carolina Ciacci	University of Salerno	Gastroenterology
Associate professor	Gerard Mullin	Johns Hopkins Hospital, Baltimore, Maryland	Gastroenterology
Doctor	Brian Berman	University of Maryland School of Medicine	Family and community medicine, integrative medicine
Professor	Basilio Malamisura	Azienda Ospedaliera Salerno	Pediatric gastroenterology
Doctor	Annamaria Staiano	University of Naples, Federico II	Pediatrics
Professor	Jost Langhorst	University Duisburg-Essen, Germany	Gastroenterology
Professor	Fabio Cominelli	Case Western Reserve University, Cleveland, Ohio	Gastroenterology
Doctor	Marina Aloï	University Sapienza, Rome	Pediatrics
Associate professor	Gabriele Riegler	University of Naples	Psychiatry
Associate professor	Marco Romano	University of Naples	Gastroenterology
Assistant professor	Jun Mao	University of Pennsylvania	Family medicine
Professor	Claudia Witt	University of Zurich Switzerland	Epidemiology, integrative medicine
Professor	Renato Gammaldi	University Hospital "San Giovanni e Ruggi", Salerno	Intensive care
Doctor	Giulio Corrivetti	Salerno Health Authority	Psychiatry
Professor	Alessio Fasano	MassGeneral Hospital for Children	Pediatrics
Doctor	Elio Rossi	Homeopathic Clinic, Hospital of Lucca	Homeopathy/integrative medicine
Title	Moderator	Institution	Medical Specialty
Associate professor	Vajro Pietro	Department of Medicine of the University of Salerno	Pediatrics
Director department neonatology	Lopardo Beatrice	Neonatology, Salerno	Neonatology
Professor	Ronald Kleinman	MassGeneral Hospital for Children	Pediatric gastroenterology and nutrition
Professor	Palmiero Monteleone	University of Salerno	Psychiatry
Doctor	Riccardo Troncone	University of Salerno	Pediatrics
Professor	Allan Walker	Harvard Medical School	Pediatric gastroenterology
Doctor	Mario Colucci	Salerno Health Authority	Infectious diseases
Doctor	Armando De Martino	Salerno Health Authority	Emergency medicine
	Stefano Pepe	Telethon Institute of Genetics and Medicine, Naples	Genetics
	Tiziana Salvati		Psychology
Title	Organizer	Institution	Medical Specialty
Professor	Brian Berman	Center for Integrative Medicine, University of Maryland School of Medicine, Baltimore, Maryland	Family and community medicine, integrative medicine
Professor	Alessio Fasano	MassGeneral Hospital for Children	Pediatric gastroenterology and nutrition
Doctor	Giulio Corrivetti	Salerno Health Authority	Psychiatry
Executive director	Susan Berman	Institute for Integrative Health, Baltimore, Maryland	
Professor	Claudia Witt	Complementary and Integrative Medicine, Zurich, Switzerland	Integrative medicine



**Figure** Components of the gut-brain axis: a schematic. Reproduced with permission from: Grenham S, Clarke G, Cryan JF, Dinan TG. Brain-gut-microbe communication in health and disease. *Front Physio.* 2011;2:94.

specific focus. IBS, inflammatory bowel disease (IBD), celiac disease, GI malignancies, and anorexia nervosa were systematically discussed in the context of pain modulated by the gut-brain axis. Each session began with a clinical case and was followed by 3 distinct types of presentations; the first described the conventional approach to treating pain in that condition, the second discussed strategies for pain control using complementary medicine, and the third offered a combined integrative approach to pain for that condition utilizing the expertise of 2 discussants, 1 from the conventional medical sphere and the other from the complementary medical sphere. This 3-step presentation model allowed for a unique forum and an open, mutually respectful dialogue among thought leaders from both the biomedical and integrative medicine communities.

While each individual session highlighted best practices for pain management in the specific medical condition being discussed, several overarching themes emerged across all sessions irrespective of disease context (Box). These unifying themes were alluded to throughout the 5 corresponding sessions and helped to create a deeper, more nuanced understanding of evidence-based biomedical and integrative strategies in managing pain modulated by the gut-brain axis.

## SUMMARY OF SESSIONS

### Session 1: Irritable Bowel Syndrome as a Quintessential Disorder of the Gut-Brain Axis

The first session discussed IBS, a functional GI disorder

quintessential of the gut-brain axis. The clinical vignette introducing IBS focused on 2 key clinical aspects of the syndrome: its variable symptomatology delineated by the Rome Criteria and the need for a tailored approach to treatment depending on the dominant symptoms. The case also elucidated the dietary connection to serotonin and other neurotransmitters: increased acetylcholine in constipation-predominant IBS and increased norepinephrine in diarrhea-predominant IBS. Conventional treatment modalities for IBS were presented including lifestyle changes, a low-FODMAP (fermentable oligo-dissaccharides and polyols) diet, psychotherapy, stress management, cognitive behavioral therapy, psychopharmacology, and pharmacotherapy such as a low-dose tricyclic antidepressant, while the integrative approach offered traditional Chinese medicine and acupuncture as potential adjunctive treatments.

### Session 2: Anorexia Nervosa as a Mind-Body Disorder

The second session introduced anorexia nervosa as a disorder of the gut-brain axis. The clinical vignette presented a young woman with classic features of anorexia and highlighted the importance of an early diagnosis and subsequent treatment using a multidisciplinary team, which included a primary care physician, psychiatrist, psychologist, and nutritionist. While several presenters mentioned the limited role that pharmacotherapy such as olanzapine or selective serotonin reuptake inhibitors could play in treatment, the majority of the discussion centered around the complex bio-

### Common Themes In Pain Management In The Context Of The Gut-Brain Axis

1. Pain is a complex disorder with numerous biopsychosocial forces involved.
2. Pain treatment requires a highly coordinated, multidisciplinary, team-based approach.
3. The patient belongs at the center of the treatment plan.

psychosocial forces involved in this condition. Interestingly, nearly all presenters approached anorexia nervosa as a mind-body disorder and offered evidence to support the use of integrative modalities such as mind-body medicine, acupuncture, traditional Chinese medicine, and homeopathy in its management.

#### Session 3: Celiac Disease and Migraine Pain: Elucidating the Crosstalk in the Gut-Brain Axis

The third session discussed the gut-brain axis in the context of celiac disease and its association with migraine headaches. Led by a case presentation, the discussion centered around the role that the gut microbiome plays in this linkage. Several proposed mechanisms of action were presented, including small intestine bacterial overgrowth (SIBO) promoting a pro-inflammatory cascade and compromised gut-immune barrier, thereby contributing to increased gut permeability and bacterial translocation. Strategies for pain management in patients with celiac disease and migraines included novel approaches like mind-body therapies, functional medicine, probiotics, and emerging vaccine formulations.

#### Session 4: Inflammatory Bowel Disease and the “Exposome”

The fourth session focused on IBD pain and the gut-brain axis. The clinical vignette described a pediatric patient with a new diagnosis of IBD and introduced disease activity indices such as the PUAIC and Pediatric Quality of Life Inventory. The subsequent discussion highlighted the management of both adult and pediatric patients with IBD. Various pathways in the pathophysiology of IBD were presented, including the microbiome, gut-immune barrier, and “exposome.” In discussing IBD treatment, presenters highlighted the fact that disease management was synonymous with pain management, since disease activity correlated directly with intestinal inflammation that subsequently led to pain. An effective strategy for disease management, and thereby pain management, in IBD was a multidisciplinary approach using conventional pharmacotherapy along with nonpharmacological approaches such as mindfulness meditation, yoga, and stress management, among others.

#### Session 5: Gastrointestinal Malignancies and Their Varied Pain Syndromes

The fifth session illustrated the gut-brain axis in the context of GI malignancies, particularly of the colon and

pancreas. In this clinical vignette, the characteristics of the patient’s neoplastic pain were complex and multifactorial: nociceptive and neuropathic pain caused by tumor growth and metastatic disease, as well as psychogenic pain related to the cancer diagnosis. Presenters discussed the conventional approach to pain management in cancer patients, which included employing an “analgesic ladder” of nonsteroidal anti-inflammatories, opiates, antidepressants, anticonvulsants, local anesthetics, celiac plexus block, and in some cases, neurolysis. There was also considerable discussion on integrative approaches such as mindfulness meditation, yoga, and acupuncture within the framework of a multidisciplinary, team-based, patient-centered approach to care.

#### Panel Discussion: Next Steps in Managing Pain in the Context of the Gut-Brain Axis

The symposium’s final session was a panel discussion on insights, lessons learned, and next steps from the day-long event. Discussants agreed that the gut-brain axis was a true paradigm shift in the understanding of chronic pain in GI illness and the symposium was an important first step in elucidating this novel yet not well-understood construct. They called for a greater need for research on the mechanisms of pain in the context of the gut-brain axis, additional research on the mechanisms of action of both biomedical and integrative therapies in modulating pain, and further studies in comparative effectiveness, including “omics” trials, to better understand whether specific subsets of patients may gain greater benefits from specific treatments.

#### CLOSING REMARKS: REFLECTIONS FROM THE SYMPOSIUM ORGANIZERS

The symposium officially concluded with closing remarks from Drs Brian Berman and Alessio Fasano. They remarked on the unprecedented nature of this gathering with respect to the type of content discussed, the range of medical specialties represented, and the rare confluence of the biomedical and integrative medical models—all for the common goal of gaining a better understanding of the gut-brain axis and its impact on pain. They reflected that while the crosstalk between the enteric and nervous systems has not yet been well-understood, its presence calls into question an outdated assumption that the mind and body, vis-à-vis the gut and brain, are separate. They encouraged the need for pragmatic randomized clinical trials, basic science research, and translational research to elucidate the underlying mechanisms of pain and its treatment, using the combination of biomedical and integrative therapies as a new approach to personalized medicine. In concluding their remarks, they stated that as the approach to understanding disease etiology is changing, so too is the approach to disease management. A multidisciplinary, team-based, patient-centered approach using the best of conventional and integrative therapies, with shared decision-making with the patient, is the future of pain therapy, irrespective of disease context.

To view or download the full-text article, visit: [www.gahmj.com/doi/full/10.7453/gahmj.2015.113](http://www.gahmj.com/doi/full/10.7453/gahmj.2015.113)