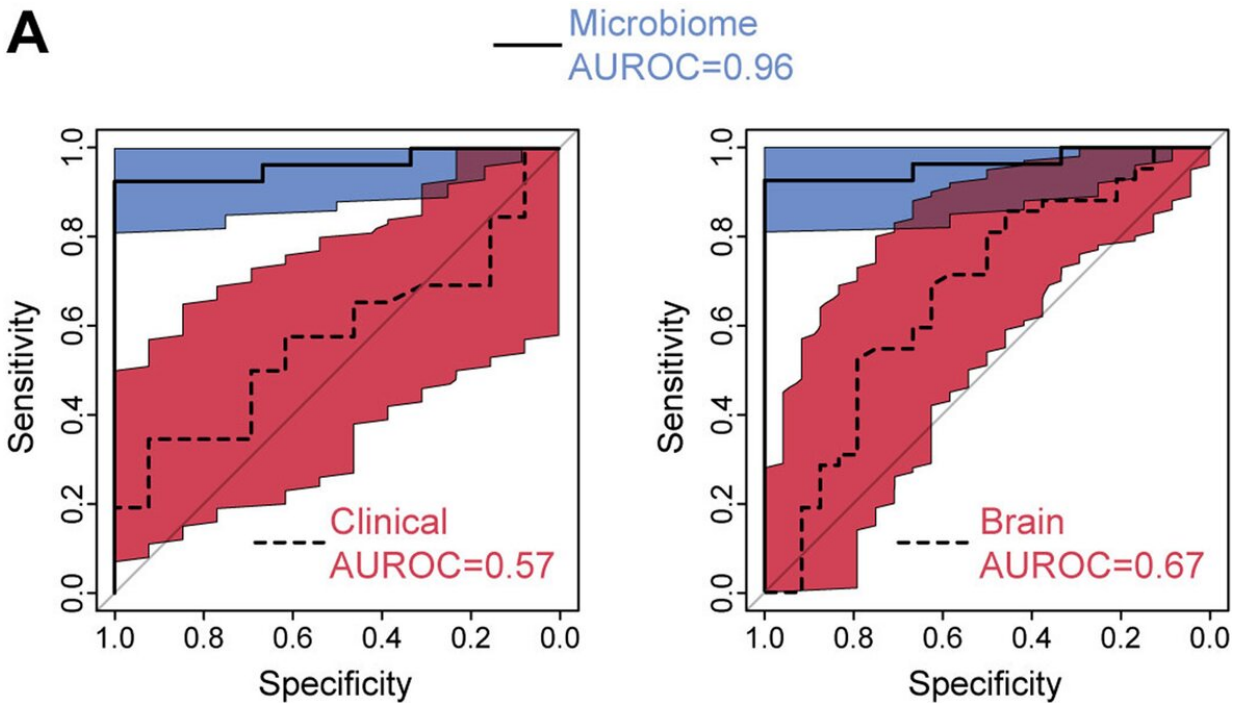


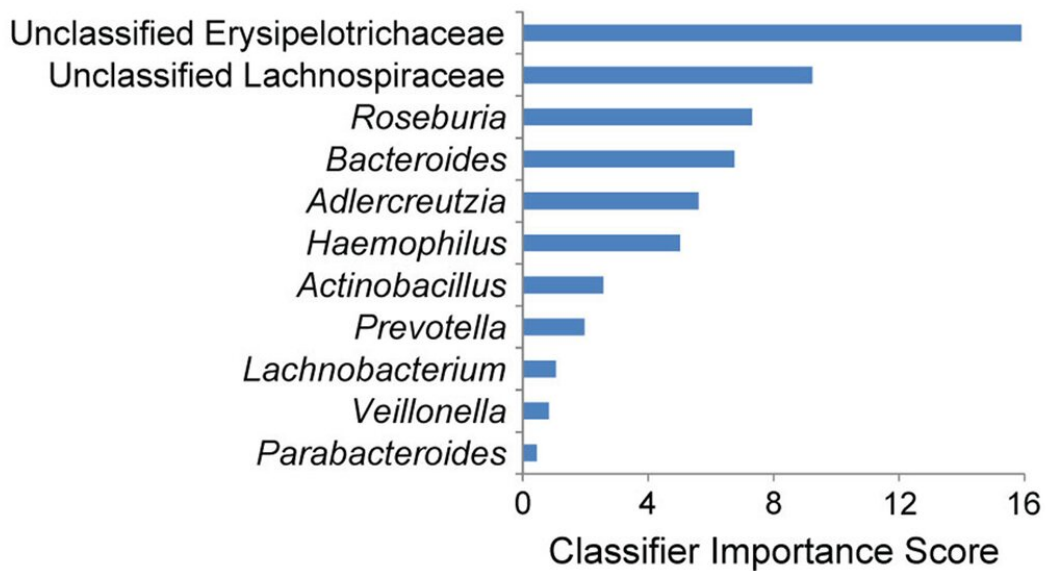
In IBS patients, cognitive behavioral therapy modulates brain-gut microbiome and helps relieve symptoms

January 31 2022, by Dirk Hoffman

A



B



Classifiers derived from baseline fecal microbiota profiles outperformed those based on clinical/demographic and neuroimaging data to predict CBT response. A Receiver operating characteristic curves of random forest classifiers for CBT response constructed from differentially abundant microbial genera, baseline clinical/demographic data (left panel), or brain data (right panel). The 95% confidence intervals are represented as colored regions surrounding these curves

(blue=microbiome, red=clinical/demographics or brain). B Importance scores for the 11 microbial genera in the random forests classifier. Credit: DOI: 10.1186/s40168-021-01188-6

A joint study conducted by researchers at the University at Buffalo and the University of California, Los Angeles is revealing for the first time that behavioral self-management of irritable bowel syndrome (IBS), a painful and common gastrointestinal disorder, can fundamentally change the gut microbiome. It is the first to show how cognitive behavioral therapy can teach patients information-processing skills that address the biological roots of their GI symptoms.

"This work demonstrates that teaching people how to think more flexibly in specific situations can reduce the physical tension and stress that can disrupt brain-gut interactions and crank up symptoms," said Jeffrey M. Lackner, PsyD, co-senior author on the paper, professor in the Department of Medicine and chief of the Division of Behavioral Medicine in the Jacobs School of Medicine and Biomedical Sciences at UB.

Published late last year in the journal *Microbiome*, this study, conceived by an interdisciplinary UB team, shows how a non-drug, non-dietary treatment for IBS induces changes in [brain function](#) and in the microbiome by normalizing ways of processing information, Lackner explained.

"These results will have a dramatic impact on understanding a gastrointestinal disease that has a significant public health burden," he said. "This is paradigm-shifting for how we understand the role of the microbiome and therapeutics that can modify its composition to treat and prevent disease."

Emeran A. Mayer, MD, an internationally known expert on the interactions between the digestive and nervous systems, is co-senior author on the paper. He is a professor in the David Geffen School of Medicine at UCLA and executive director of the G. Oppenheimer Center for Neurobiology of Stress and Resilience.

"Dr. Lackner's collaborative project with UCLA is an important breakthrough in the understanding of how [cognitive behavioral therapy](#) can alter brain-gut interaction to provide relief for IBS patients," says Allison Brashear, MD, UB's vice president for health sciences and dean of the Jacobs School. "This study's translational research provides new hope for those afflicted with this debilitating disease."

The study was funded by grants from the National Institute of Diabetes and Digestive and Kidney Diseases to Lackner and Mayer, UB's Office of the Vice President for Research and Economic Development and UB's Genome, Environment and Microbiome (GEM) Community of Excellence.

"The findings are the first to demonstrate that a specific type of cognitive behavioral therapy developed at UB that teaches information-processing skills can modulate key components of the brain-[gut-microbiome](#) axis in some of the most severe IBS patients," said Lackner.

Learning-based treatments

"We know that the gut microbiome is a key to regulating brain-gut interactions and plays a role in overall human health from metabolism to immunity. We also know learning-based treatments like cognitive behavioral therapy are some of the most robust treatments of any kind for what is the most prevalent GI (gastrointestinal) disease, even when they are home-based delivered with minimal doctor involvement," said

Lackner.

"What we didn't know is how those two facts interact," said Lackner.

"We didn't know whether symptom relief following CBT depends on the microbiome environment to achieve its effects.

"This study is important because it reveals a precise microbiome signature that distinguishes patients who respond positively to a drug-free treatment and those who don't, and that signature corresponds with objective changes in brain function," he added.

"The fact that we see patient-reported GI symptom improvements that correspond with 'objective' biological changes in the microbiome and brain function is pretty remarkable given that we focused on a low-intensity, home-based behavioral treatment and not medical therapies like probiotics, prebiotics, postbiotics, antibiotics, and fecal microbiota transplantation known to manipulate our microbiome," Lackner said.

Eighty-four IBS patients were recruited from the parent CBT trial—the Irritable Bowel Syndrome Outcome Study, a landmark, National Institutes of Health-funded clinical trial led by Lackner that has transformed the way IBS is understood and treated.

The 84 participants underwent neuroimaging and detailed clinical assessment at clinical sites at UB and Northwestern University. UB also collected [microbiome data](#) through fecal sampling from 34 of the patients.

Eligible patients were randomized to receive 10 sessions of clinic-based CBT or four sessions of largely home-based CBT with minimal therapist contact over a 10-week acute phase. Both treatments were developed at UB.

'Boundary-breaking translational research'

"This trial was enormously complex in that we collected symptom data across different sites at pre-treatment and post-treatment," said Lackner, who sees patients at the Behavioral Medicine Clinic at UBMD Internal Medicine. "Because we were also collecting biological data at multiple times, it required a high level of precision and project management unique among major research centers. It really speaks to our division's capacity to support boundary-breaking, novel translational research with high impact potential."

UB partnered with the David Geffen School of Medicine at UCLA and the G. Oppenheimer Center for Neurobiology of Stress and Resilience at UCLA.

"All that data had to be expertly analyzed and that is where we were able to draw from the expertise of our long-standing collaborators at UCLA, experts in microbiome and imaging research," Lackner says.

UB developed the treatment, delivered it and collected data, while UCLA analyzed gut [microbiome](#) and neuroimaging data.

"It is a great example of team science between two outstanding research facilities with unique synergies," Lackner says. "There's a lot of reasons why this type of study hasn't been done up to now, but we were able to leverage our unique clinical expertise and our clinical research infrastructure and UCLA's expertise."

Of the 84 participants in the trial, 58 were classified as CBT responders and 26 were classified as non-responders.

While there were small pre-treatment differences between brain network connectivity for responders and non-responders, the significant

difference was how much the connectivity changed after treatment.

Responders showed greater baseline connectivity than non-responders between the central autonomic network and the emotional regulation network, according to the study.

Lackner said that the findings raise the possibility that CBT-responsive IBS patients can be identified in clinical practice using microbial biomarkers, before less effective treatments are initiated at great expense to the patient and health care system.

"The pattern of data may explain normal versus abnormal gut function and just how the brain-gut can influence symptoms and the relief of them," Lackner says. "Larger studies are needed to characterize the functional correlates of gut microbial changes and to identify distinct subtypes of IBS patients for whom brain- and gut-directed therapies are most effective.

"This is an example of science moving away from a 'one-size-fits-all' brand of medicine toward a more personalized medicine approach driven by translational research."

More information: Jonathan P. Jacobs et al, Cognitive behavioral therapy for irritable bowel syndrome induces bidirectional alterations in the brain-gut-microbiome axis associated with gastrointestinal symptom improvement, *Microbiome* (2021). [DOI: 10.1186/s40168-021-01188-6](https://doi.org/10.1186/s40168-021-01188-6)

Provided by University at Buffalo

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