**Transcript Details**
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/crohns-colitis-foundation-perspectives/our-evolving-understanding-of-pain-in-ibd/11257/

**ReachMD**
www.reachmd.com
info@reachmd.com
(866) 423-7849

---

Our Evolving Understanding of Pain in IBD

Announcer:
Welcome to Crohn's & Colitis Perspectives on ReachMD, produced in collaboration with the Crohn's & Colitis Foundation

Here's your host, Dr. Matt Birnholz.

Dr. Birnholz:
Our understanding of pain in IBD is rapidly evolving. According to recent research, up to 70% of IBD patients present with pain at the onset of disease or during disease flares, but many patients go on to report ongoing pain even when their disease is in remission. This has created an explosion of interest in research into brain and gut connections in IBD, and it's these connections that will become the focus of today's discussion.

Welcome to *Crohn's and Colitis Foundation Perspectives* on Reach MD, coming to you from the third annual Crohn's and Colitis Congress in Austin, Texas. I am Dr. Matt Birnholz, and here with me is Dr. Emeran Mayer, a gastroenterologist and professor of medicine at UCLA's School of Medicine. Dr. Mayer is also a neuroscientist and serves as executive director of the UCLA Center for Neurobiology of Stress and Resilience and he is one of the leading investigators in the world on brain and gut microbiome interactions in GI disorders, including IBD. It is a topic that is literally exploding on the map and getting much attention at this year's conference. So, Dr. Mayer, welcome to the show.

Dr. Mayer:
It's nice to be on the show.

Dr. Birnholz:
Great to have you with us. So, to start off, can you just give us an overview of where we stand in understanding how this gut and brain access is affected or altered in IBD?

Dr. Mayer:
It's been obvious to us in our center for at least 20 years that there must be a communication between the brain and the gut in IBD, not just in IBS; but the field, other than the patients, was not really ready for accepting this. This was considered an immunological disease of the gut. So, in principle, there's no organ in the body that has such close connections with the brain as the gut, and there a long reason are many reasons for that: evolutionary, but also in terms of you know functional regulation. The gut has its own nervous system, the so-called enteric nervous system, which deals with simple things like peristalsis and fluid secretion, but this little brain in the gut does not does not really link the gut to other higher functions such as pain, emotion, motivation, and that's really, I think, what has made this so interesting; that if you think about pain, most people think about pain as an injury on the nerve ending that that hurts, like typical acute pain. In IBD, we have really been dealing mainly with chronic pain, a very different entity, and every part of the brain-gut (I would say now also the brain-gut-microbiome axis) is involved in the generation and maintenance of that pain. So something that may start in the periphery due to acute inflammation makes its way by sensitization of pathways to the spinal cord, from the spinal cord up to the brain stem, from the brain stem to higher centers, and then the brain doesn't just sit there, but it responds, trying to modulate this pain, and typically, in chronic pain, to down-regulate it. This is a pretty sophisticated process, and in humans, it is difficult to dissect all these components, but we believe from and from our research so far that this brain-gut axis is altered. The brain is altered in chronic inflammation in IBD. We just presented a study here that this alteration affects both the structure and the function of the brain, and that the brain, as shown earlier, has powerful ways of modulating the perception of pain, and we think that is also altered in some patients with IBD who have more pain than you would expect from their inflammation.


© 2023 ReachMD

Dr. Birnholz:
That's great. Why don't we dig a little bit further into the triggering of pain, because it seems that pain in IBD is triggered from a variety of sources, including but not limited to inflammation itself. You have psychosocial factors, stress, and anxiety. Can you just speak to the diversity of pain triggers and its relevance to the gut and brain axis as we know it now?

Dr. Mayer:
Yea, let's start with inflammation. For most people, it's the most obvious and intuitive. And we have hundreds of animal models. We, you know, cause inflammation in the colon, small intestine; we study the nerve endings, you study the dorsal root ganglia, you study the spinal cord all the way up, and you will find a time-course sensitization in the periphery that lasts only really a relatively short time until your peripheral nerves are sensitized. That sets off the spinal cord. The spinal cord memory of pain stays longer, and then it goes to the brain and then the brain decides what it is going to do with it. Is it going to amplify it? Because certainly one advantage of the brain amplifying it is that you know it right away and can do something about it. Or, if it's chronic and it has been there for a while, the brain tries to suppress it, and it has multiple mechanisms, so-called descending pain modulatory mechanisms. Personally, I think that is probably one of the most important parts in those patients who have had chronic pain, and the pain persists even when the inflammation is treated. So, there has got to be a central mechanism that drives that. So, I think we have made lots of progress in that. Most recently, there are also the gut microbes that have come into play. So gut microbes produce a lot of metabolites and some of these metabolites can interact with different levels of this pain system - tryptophan metabolites, serotonin, kynurenine. Kynurenine, for example, (one of the tryptophan metabolites) has been shown to modulate many brain circuits involved in emotional brain regulation. So it has gotten more complicated, so now we don't just have the inflammatory molecules- the cytokines and so forth- but we have these chemicals that proven are working parallel with the traditional cytokines and inflammation mediators.

Dr. Birnholz:
Well, for those just tuning in, you are listening to *Crohn's and Colitis Foundation Perspectives* on ReachMD. I am Dr. Matt Birnholz, and today I have the pleasure of speaking with Dr. Emeran Mayer about pain and the gut-to-brain axis in IBD. So, Dr. Mayer, you've given us a great foundation now on the underpinnings between this brain and gut connection for pain signaling, but if we translate that to clinical practice, how can these understandings be better utilized to care for IBD patients who are experiencing pain? How do we help counsel them? How do we actually make treatment recommendations that will help them counter this system that has kind of gone-off-the-rails dealing with a chronic pain situation?

Dr. Mayer:
So I would say there are two types of patients. The patients who are in a flare, it's kind of appropriate that they have the pain. I mean, that's part of the flare; it's the main component and we have IBD treatments that deal with the flare, so in the ideal patients, you treat the flare with whatever medication approach, and the pain will go away. It becomes a problem in those patients where this does not happen. So you treat the inflammation, you can take biopsies, do a colonoscopy. The mucosa seems to be healed, but the pain persists. That's a significant portion of patients. I forgot the exact number – it's somewhere between 20-40% of Crohn's patients. And then, sort of a major problem starts or some physicians would then say, "Well, this wasn't this wasn't the right biological therapy. We have to change; we have to increase the dose." So that's a big mistake, because this is basically saying, "It doesn't respond because it's we are not hitting it hard enough." I don't think that's really the case. I think physicians have to think about it – okay, so then it's a different mechanism. And what can we do in that case? Make an assessment. Are there other factors that can be addressed clinically that may, you know, may play a role in this? So clearly, psychosocial factors play a role in this. So anxiety, symptom-related anxiety, is a big one. You don't have to be anxious in general, but you always worry about your symptoms. Catastrophizing is another one. There's also, now recent studies we have found that you can divide up patients with IBD (we've done this on a large number) into a stress hyperresponsive group and a normal responsive group. The stress hyperresponsive group has a different perception of stress. It goes, again, to the salience assessment. Those patients, if you followed them for three months, they had more flares. They were the same at baseline, but if they had this phenotype, they had a greater number of these flares. So this phenotype, or this subgroup, can easily be identified in the clinic. I mean, this could be either a short questionnaire or it could be…. We are interested in studying the biology behind it, but for the clinician, you can make that assessment. You don't even need a psychologist to do that. So if you have a patient like this, you have to add, you know, an adjuvant therapy to your regular IBD targeted treatment, and there is a range of things. I personally prefer a pharmacological one: so there are the same medications we try in IBS, so you try low-dose tricyclic antidepressants – not for depression - but if the patient has clear-cut anxiety or depression, clearly that needs to be treated. Then there's the nonpharmacological, which is a kind of wide range today, which could be mindfulness-based stress reduction. So, learning of how not to over-respond to stress. There's cognitive-behavioral therapy, and the interesting thing with that is that used to be a fairly limited access, because it's expensive, it's long-term. Most cities don't have a CBT or GI-CBT specialized person, and that's rapidly changing. So, there are now several companies (most recently announced, Mohana), that developed these web-based CBT programs, and the physician would just write a prescription, and the patient, you know, gets online. There are already studies from England that this is


© 2023 ReachMD

highly effective, as effective as face-to-face therapy. So, I think we have a range of things available. It will require a significant amount of education on the physician's side, that these things are available. They are not just psychological treatments or biological treatments aimed at a biological organ, the brain, but I think this could make a huge difference. It's not that challenging for the physician, for the gastroenterologist. If you think about this on-line CBT, I mean, this take two minutes to explain and write a prescription.

Dr. Birnholz:
But getting through the stigma that patients will sometimes feel in potentially being prescribed a psychotropic or being prescribed CBT, thinking, "Oh, so you're telling me I'm just an anxious person and my pain needs to be mitigated because I'm just anxious. I mean, this is pain I'm feeling." So, it sounds like there is an education component counseling-wise, to be able to say, "This is treating the biological neurochemical root that is keeping your chronic pain going, even when you're in remission. This is a potential way to treat that, without us jumping the gun on your treatment which is working otherwise. Your flares are taken down." Is that part of the counseling that has to go into this?

Dr. Mayer:
That's part of the counseling and you know, there is obviously a long way to go from a traditional – I still remember, even in our division, you know, when I gave a talk on this topic, and some senior IBD expert would get up and say, "I just want our fellows not to get confused here, you know, IBD is a real disease. It's not psychological." So this was, you know, five years ago. It has changed. A lot of the younger people are really aware of this and particularly patients - this to me is surprising – you know, patients are really aware of it. We're not saying that somebody has fistulating disease and, you know, resections, and that you can cure anything or that this is a psychological problem. But if you deal with the patients that were recent onset, frequent flares – this group, 20-40% group that has persistent pain with reduction of inflammation - they are very open to that. I mean, with education on both sides, physician and patients, is key.

Dr. Birnholz:
And is there a role for referring to pain specialists or other specialists, for instance, if comorbidities are involved, or does this ultimately all fall on the IBD specialist, to be able to incorporate these tools and to really get them utilized more often in practice?

Dr. Mayer:
I would say that certainly based on my experience, pain experts are not really experts on chronic visceral pain, just like psychiatrists are not experts. So our division has responded to this by creating a wellness program with a wellness coordinator, a nurse practitioner. If you the physician refer that patient to that wellness coordinator, she will explain all the things that I just tried to explain to you and she is very popular; patients love the explanation. Then she divides and triages it too, we also now have a cognitive behavioral therapist in the division but also outside in close vicinity, and I think that's the ideal model. If an institution can afford that, I would say, and there are a few universities now in the country that have started to do this: there's Michigan, there's Mount Sinai, UCLA. And I think you will become the model. It's more cost-effective than the current one.

Dr. Birnholz:
We are, unfortunately, out of time. But I very much want to thank my guest, Dr. Emeran Mayer, for joining us today to talk about the brain and gut axis and the connections to our deepening understandings of pain in IBD. Dr. Mayer, it has been fantastic having you on the program. Thanks so much.

Dr. Mayer:
It was a pleasure to be on the show. Thank you.

Dr. Birnholz:
For ReachMD, I'm Dr. Matt Birnholz. Thank you all for joining us.

Announcer:
This program was brought to you in collaboration with the Crohn's & Colitis Foundation. If you missed any part of this discussion, or to find others in this series, visit ReachMD.com/foundation, where you can be part of the knowledge.


© 2023 ReachMD