00:00:02:13 - 00:00:09:16
Speaker 1
Hello and welcome. I'm Claire, and you're listening to Microbe Talk. The podcast by the Microbiology Society.

00:00:11:18 - 00:00:42:14
Speaker 1
The Gut Brain Axis is a link between the mechanisms of the gut microbiome and the activity of the brain. It's a two way communication via chemical signals, such as neurotransmitters and hormones. Changes to the composition of the gut microbiome can affect the way in which the brain is able to function. And from the University of Alberta, wanted to find out more about how medications for bipolar disorder could affect the gut microbiome and therefore affect the brain.

00:00:43:08 - 00:01:14:23
Speaker 1
So they collected and reviewed data from existing studies and published their systematic review in microbiology. I invited Dan onto Microbe Talk to Dig Deeper into their paper, the field of study and the importance of reviewing existing datasets. Hi and welcome to Microbe Talk. It's lovely to speak with you. Good place to get started with is. Could you please introduce yourself, your institution and what research you're up to?

00:01:16:07 - 00:01:51:19
Speaker 2
So my name is An. I'm from the University of Alberta. I'm currently going to my fourth year as a PhD, students in psychiatry and my main research, mostly focuses on stroke and treatment and recovery. But as part of as a student of the Department of Psychiatry, I also do some research on mental disorder and other psycho psychological disorders that we have.

00:01:52:05 - 00:02:26:10
Speaker 1
Amazing. And yeah, the reason why I invite students card today is I came across your paper, Pharma's Psychiatry and gut microbiome, a systematic review of the effects of psychotropic drugs for bipolar disorder published in microbiology. I saw that paper and my interest immediately piqued. There's lots to kind of unpack there. But before we get into the like really interesting nitty gritty parts of your paper, could you just start us off with a very brief overview as to what the paper's about?

00:02:27:09 - 00:03:11:16
Speaker 2
Yes. So the paper is about investigating how our current in drug treatment for bipolar can modify gut microbiome composition in bipolar patients. Because recently there's a lot of papers coming out saying that the gut microbiome of bipolar patients are different than healthy people. So we were interested to see whether introducing drugs flow for a brief period or over a long period of time could have some effect in that connection.

00:03:11:22 - 00:03:31:23
Speaker 1

Awesome. So I kind of keep up like aspect of this paper is obviously talking about the sort of gut brain axis and how the gut and the brain are connected. It's quite is quite an overwhelming thing to to the kind of attack. And it's you give me like an overview of what the gut brain axis is.

00:03:33:03 - 00:04:11:12
Speaker 2
Yeah. So only that very recently that we started having a lot of interest into the gut brain axis. So a very brief overview is that the gut and the brain are connected. We have the gut brain axis which refers to like when you have changes in the nervous system, for example, when you're in stress and your body releases cortisol, for example, that can affect the functions of the gut.

00:04:11:12 - 00:04:58:03
Speaker 2
So cortisol can can cause like leaky gut, which increases gut permeability. So that is one example of how the gut and the brain are connected. Of course, there are like other molecules that can be at play, for example, other neurotransmitters. So when you have a psychological disorder or mental disorder like schizophrenia or depression or bipolar, in this case your levels of neurotransmitters like serotonin or dopamine can fluctuate, can, can, can, can be different from healthy controls.

00:04:58:03 - 00:05:04:06
Speaker 2
And that kind of changes can affect the way the gut functions.

00:05:05:05 - 00:05:17:11
Speaker 1
Yeah. So from you've put it across perfectly that where you've got kind of two examples. So from this examples, I mean does it happen in both directions that gut affects the brain and the brain affects the gut?

00:05:19:09 - 00:06:16:02
Speaker 2
Yes, absolutely. There is also. So so I only brought up examples of how the brain affects the gut and how the chemicals in the brain affects affect the gut, but also, it's it also happens the other way around. So, for example, a very, very simple example is when there are people who are lactose intolerant or people who are allergic to something like lactose or gluten and taking in those kind of products can increase gut inflammation and that can release certain chemicals that can also affect the brain in the way our in our moods or in our energy level.

00:06:16:15 - 00:06:35:13
Speaker 2
Sometimes that can make us fatigue. That's why I like the Mediterranean diet is suggested by a lot of doctors and physicians who are treating people with chronic gut inflammation or other metabolic problems.

00:06:36:01 - 00:06:51:15
Speaker 1
Hmm. Interesting. And back to your your review. Could you explain how you went about it, what kind of inclusion criteria you looked into and what I suppose we all main findings.

00:06:52:10 - 00:07:37:10
Speaker 2
One So our inclusion criteria was we wanted to look at experiments or trials in humans that have used the bipolar treatment. So we have a list of current drug treatments for bipolar. So that includes like mood stabilizer, antipsychotics, lithium, etc.. And then we looked at the studies that measure outcomes after bipolar treatments and compare that to baseline, and we only came up with a few handful papers.

00:07:38:03 - 00:08:10:19
Speaker 2
So that was pretty interesting. That suggests that the field was still relatively new and the studies that we looked at, they are quite diverse in terms of their methods and the technologies that they use. So some studies, some study use sequencing and some study look at the the bacteria culture from the gut microbiome of patients being treated with medication.

00:08:10:19 - 00:08:51:16
Speaker 2
And also we also saw a very diverse drugs that were used. So it's not just like an array of medication that were used consistently through all the groups. And we also saw that the studies are were distributed all across the world. So there was one in Japan, some in the US and so, so so that was really interesting that there were all these studies done across the world and no one has looked that synthesizing those.

00:08:52:00 - 00:09:42:17
Speaker 2
And I found that quite important because given that it's a new field and there hasn't been much done, it's important to synthesize those results, to give directions to future studies and for the results we like. Again, because of such diverse methods and technology being used, we also found very, very diverse results. So one line that we could conclude was that the bipolar drug treatment definitely alter the gut microbiome composition of bipolar patients.

00:09:43:14 - 00:10:41:14
Speaker 2
And compared to baseline before they were having before they started taking medications. And also there there was certainly this division of bipolar medication, responder and nonresponders. So the people who responded well to medication indicated by their improved depression symptoms after treatment, they seemed to have a gut microbiome composition very close to similar to healthy control. So that points to like disconnection of how like symptoms, improvement and recovery can be related to microbiome composition.

00:10:42:09 - 00:11:14:10
Speaker 1
Hmm. Really exciting, I suppose. It's a tale of two sides, isn't it? When you have a small sort of data set, it's. It's exciting because it means that you're at the beginnings of everything, but that it's also like, Oh, okay, this is all all over the place. It's quite hard to pin it down. And one thing I just wanted to also address, could you explain like what bipolar disorder is and currently like what is the status of the way in which we treat bipolar disorder?

00:11:15:02 - 00:11:22:08

Speaker 1
What characterizes bipolar disorder, and where maybe the improvements might need to go?

00:11:22:13 - 00:12:01:14
Speaker 2
Okay. So bipolar disorder, before it was called manic depression, and it's usually characterized by extreme mood swings, but sometimes the mood swings and doesn't happen. It doesn't have to be so extreme. So there the mood swings include mania, which is an emotional high and and depression, which we probably all familiar with. So and and there's also hypomania, which is less extreme than mania.

00:12:01:14 - 00:12:40:14
Speaker 2
So patients who are diagnosed with bipolar disorder will go through these mood swings. In some case, very extreme. The symptoms can include, like other than feeling consistently sad, there's also like feeling hopeless, suicidal, lethargic, and those kind of like sleep and appetite, which yeah, very much in negates treatments. So the current treatments that we have for bipolar patients are mostly medications.

00:12:40:20 - 00:13:16:19
Speaker 2
So there's a whole range of medications that can be prescribed for bipolar patients. So that includes antipsychotic lithium, mood stabilizer. And one of the problems that we encounter in treating bipolar patients is that there's a high rate of relapse and sometimes medications are not effective and sometimes it can take patients a while to find the right medication.

00:13:17:01 - 00:13:20:09
Speaker 1
So just so, what do you mean by relapse? Sorry.

00:13:21:02 - 00:13:38:23
Speaker 2
So after even taking medications, a patients can still fall back into like depressive or manic or hypo manic symptoms even after a period of stability.

00:13:39:06 - 00:13:47:24
Speaker 1
Got you. Got you. Okay. So it can work for a bit. So then as you were saying, it's like about it's difficult to find the right course of treatment.

00:13:48:06 - 00:14:23:21
Speaker 2
Aside from like having to find the right treatment to work for you in managing the symptoms. There are also like very big side effects. So for anti-psychotic one of the biggest side effects that were reported by patients are metabolic disturbance. So weight gain, any changes in like just metabolic functions.

00:14:24:03 - 00:14:41:21
Speaker 1

So there's this sort of whisper, I suppose, of how the gut microbiome might play a part in the different ways that people respond to medication. So is that what inspired you to undertake this review, to sort of iron out what that connection is? I suppose?

00:14:41:21 - 00:15:22:12
Speaker 2
Yes. So I was really I was taking a course from Dr. Andy Grimshaw and we talked a lot about other psychiatric disorder out there in my lab. We used to do a lot of studies on schizophrenia disorder. So mood disorder was one of those subjects that I was interested in. And because I work in a lab where we test a lot of medications, I was also interested in how medication use can affect treatment response.

00:15:23:10 - 00:15:40:08
Speaker 2
What we found in our paper was exactly what I was curious about, which is that medications have different effects on certain people and gut microbiome reflects that in a way. Or effects that we just don't know yet.

00:15:40:08 - 00:15:51:12
Speaker 1
Yeah. Yeah. And what would you say was the most interesting or the most surprising thing that you found whilst carrying out your review?

00:15:51:12 - 00:16:38:19
Speaker 2
I think the most interesting is that we see that return to baseline of microbiome composition in treated patients who responded well to treatment. That was really interesting. I was I only hypothesized that that treated bipolar patients will have a different composition to untreated and healthy control. But I didn't expect it to like return to baseline and that was interesting because they saw that kind of return to baseline both in brain images, both in gut microbiome, and also depressive symptoms.

00:16:39:03 - 00:17:05:10
Speaker 2
So you see a piece of brain, a piece of gut, they are connected in a way. And I'm very curious to see how that all works and the mechanism in it. But I guess we just haven't got enough studies to decipher that yet.

00:17:06:00 - 00:17:23:17
Speaker 1
And you actually led very nicely into, you know, there's still so much more to find out. What were your sort of thoughts and recommendations be for the future of ironing out this gut brain connection and patients with with bipolar disorder?

00:17:24:17 - 00:17:54:08
Speaker 2
I think in the future. So right now, all the studies that we have are comparing patients who were treated for a period of time to their baseline pain and compare that to the healthy control. And we haven't got the naive treated patients yet. So bipolar patients who were treated with a sugar pill and that was carry on for a long time with blinded control, obviously.

00:17:54:14 - 00:18:32:05
Speaker 2
And then that would be compared to the treated bipolar patients with the actual medication. And that's the way that we can see if there's a causal effect or if there's any other effect is to include naive treated patients. But that can introduce certain ethical problems, as you can't deny a patients who are struggling with this kind of mental disorder the right medication.

00:18:32:21 - 00:19:15:12
Speaker 2
So definitely it can be a big challenge in the future. But we could start with animal models of bipolar disorder and then we could then manipulate include both treated and non treated groups and we can follow them through the course of treatment and see if their gut microbiome composition changes. But to have more relevant, more impactful effects, we definitely still have to look at the human models.

00:19:15:12 - 00:19:20:23
Speaker 2
But like I said, that can introduce a lot of ethical problems.

00:19:21:01 - 00:19:35:01
Speaker 1
Mm hmm. And you've told us a little bit about where you'd hope research would go in terms of, like, far in the future. What could this lead to in terms of how we treat bipolar disorder?

00:19:35:01 - 00:20:10:09
Speaker 2
And that's really interesting because in the future, if we find out that whether whether gut microbiome affects human response or if we have a causal relationship that can be inferred in the future studies, we could really change the way that we treat bipolar patients. So right now, we rely heavily on medication there and there are some piece of psychological counseling in there.

00:20:11:03 - 00:20:55:23
Speaker 2
But in the future, if there's a causal effect, it might be important to introduce some supplementary metabolic treatment. So for example, taking probiotic or prebiotics or having certain like treatment like FMT, which is fecal microbiota transplantation, if we found out that that, that there is a causal effects, those are the possible directions that maybe we can take. It's not like I'm, I'm not recommending that now is just an idea.

00:20:56:04 - 00:21:14:15
Speaker 1
Of course it's a needs a huge research that ahead of time and am and one of the things that was quite interesting that came up there was a particular set of results that looked at gender differences. So could you tell me about the.

00:21:14:21 - 00:22:06:00
Speaker 2

Sex differences are becoming very popular or important in the research community because historically studies were designed and results were collected based mostly on males. So a lot of our treatments were tailor to males or designed based on results that were collected on male participants. So that was something interesting that we found that there's a significant changes in certain microbiome in females, but not males after treatment, and that can have many different implications.

00:22:06:11 - 00:22:09:21
Speaker 1
Oh yeah. It could undo so much of that.

00:22:10:02 - 00:22:38:21
Speaker 2
Yeah. So one way I could think of is that maybe we could target those certain bacterias to improve outcomes in females, or we could just like look more closely into those bacteria to expand on those results and see how these bacteria work. How are they making these differences in females?

00:22:38:21 - 00:23:00:03
Speaker 1
Yeah, because it opens up a whole new door of possibilities, doesn't it? It's almost like previous research is almost done with your hands tied behind your back. If there's like this aspect of the microbiome that could be such an important variable in these kinds of research. So I suppose it opens up a massive avenue of different ways you can look at this, this topic.

00:23:00:06 - 00:23:00:19
Speaker 1
Yeah.

00:23:00:19 - 00:23:41:07
Speaker 2
And also a lot of of the studies you sequencing in a problem that we usually have with sequencing data is that you end up with this massive amount of data and there's you don't know which pattern or trend to focus on. You just have a lot of data. So you're reporting all this and it's important to have this piece where where would you find the patterns or the trend across multiple data?

00:23:41:11 - 00:24:00:04
Speaker 2
Because one study can have a really I would say like confusing data just because of how big they are. So finding that trend or that pattern is very important in research, especially in sequencing data.

00:24:00:05 - 00:24:29:13
Speaker 1
Yeah, absolutely. And then there's the importance of the work that you've done and published in microbiology is the importance of a review to be able to collect that data and analyze it for things that might not necessarily be relevant to that particular study at that time. So yeah, could you tell me a little bit more about like what you think about the importance of having reflecting back and looking at reviews and looking at the existing data.

00:24:29:16 - 00:25:20:06
Speaker 2
In every field in research, reviews are very important because that's where you look at trends and you synthesizing all these data, all these details that a researcher might have not looked at before because they are not relevant or interesting to their research focus at the moment at these so reviews can provide these string that other people other the researchers can look at and that might be a new avenue or that might be relevant to their current research that they want to either expand on or start a new research project in.

00:25:21:01 - 00:26:00:19
Speaker 2
So and also review paper I think provides a very comprehensive just overview study of this topic. And sometimes that can be very helpful to someone who is new to the field and wasn't going to go through like hundreds of papers of original research with a lot of data on it. So review papers come in neatly in that sense, like providing someone just an overview of what has been done in the field.

00:26:01:05 - 00:26:19:12
Speaker 1
Yeah, absolutely. And of course, with your paper being across kind of multiple fields, like multiple fields, psychiatry has involved medicine and then microbiology. Having that review that encompasses those different things is vital. It's really important. Yeah.

00:26:20:07 - 00:26:57:11
Speaker 2
Yeah. So I remember previously, a couple of years ago, we only started thinking about gut microbiome and the brain and how they are connected. So seeing it so well developed now, it's very, very interesting because like if you think of like ten, 20 years ago, the connections between the gut and the brain weren't very much looked at. And now we have so many new targets for medicine.

00:26:57:11 - 00:27:00:01
Speaker 2
So that is really interesting to me.

00:27:00:15 - 00:27:11:12
Speaker 1
So and so how did you find that coming from your neuroscience background and attacking and analyzing microbiological aspects? How did you find that?

00:27:12:10 - 00:28:01:17
Speaker 2
So in neuroscience, you look at you looked at the bi biology piece a little bit more than the clinical side. So you read and you study a lot with animal models just so that you can closely examine the biology biology piece. So coming from that, just looking at like just looking at a whole host of different experiments. And now I'm looking at human datas and imaging and how psychological assessments are conducted or all of the modalities that we don't have in animal studies.

00:28:02:10 - 00:28:37:09
Speaker 2
That is very interesting to me. We cannot like ignore the animal study. Of course, they are very important in the way of setting the foundation for clinical and human studies. But I, I find, yes, clinical studies are, are incredibly impactful, of course, because that's where we find treatments, new treatments for our population. I wouldn't say one is better than the other.

00:28:37:20 - 00:29:24:14
Speaker 2
It's just very different. And they complement each other very well. And we now have this talk in the research community about the importance of translational research. So making sure that animal studies results from animal studies do translate and can be meaningful in human studies. So designing animal studies with human studies in mind and also when you have certain results, interesting results in human study, you bring it back to animal study to design complementary studies or follow up studies.

00:29:24:14 - 00:29:36:12
Speaker 1
Amazing. Yeah. And it's so interesting to hear your insights on that and it's been such a pleasure to speak to you and pick your brain about such an interesting topic.

00:29:36:16 - 00:29:38:01
Speaker 2
Well, thank you for having me.

00:29:38:02 - 00:30:06:18
Speaker 1
Thank you so much. It's been a pleasure. Thank you for joining me on Microbe Talk. It was so interesting to find out more about the complex area of research. If you'd like to read Anne's paper in full, you can find the link in the description you've been listening to Microbe Talk. If you like this episode, please leave a like or a comment wherever you're listening.