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### Cutting Edge Treatments for Depression in Children

#### Male Speaker:

You are listening to ReachMD, the channel for medical professionals. This segment is made possible by an educational grant from Shire Pharmaceuticals. Welcome to Updates from the Mayo Clinic, focusing on primary care, pediatrics and child mental health. Here's your host, Dr. Peter S. Jensen, a childhood and adolescent psychiatrist and Professor of Psychiatry at Mayo Clinic in Rochester, Minnesota.

#### Peter Jensen:

Welcome to ReachMD's Mayo Clinic Update on primary care child mental health. This is Dr. Peter Jensen, your host. I am particularly delighted today because I have one of my colleagues and friends that I've gotten to know over the last four years since I've been here at Mayo Clinic, Dr. Chris Wall. Welcome, Chris.

#### Christopher Wall:

Thanks, Peter. It's nice to be here.

#### Peter Jensen:

Well, we're going to be doing a really hot topic today. Dr. Christopher Wall is Assistant Professor of Psychiatry and a child psychiatrist. He's one of the hospital psychiatrists, he's on the Depression Research Center and has been involved in just some wonderful cutting edge research that he's been teaching me about since I've been here at Mayo Clinic. Chris, you know, we have a series of related persons that we've been interviewing, including a couple of yours and my colleagues. Dr. John Huxall with conversations about what are best treatments for depression. And Dr. Paul Corcan who's been talking about the biology of youth depression. But you know, one of the things that we've learned and we want to maybe tackle a topic that's kind of in the middle of those other two. That has to do with this whole issue of new and emerging treatments.

Of course, we've learned from Dr. Huxall that our treatments aren't always that great. We've heard that SSRIs are used and therapies like CBT and IPT. But we've learned that they may not work all that well necessarily for a lot of the kids. Maybe only half really are pretty well off a year later, actually back to normal functioning. So, I'm going to throw a tough one at you. Why do you think these current treatments, why aren't they more effective?

#### Christopher Wall:

Well, it is a tough question. In the years that I've been working with kids that come into the hospital as well as in our outpatient practice, one of the things that has become pretty clear is that not all depression is created equal. Sometimes we try to treat depression as though it's a single entity, but really it's pretty different from one kid to the next. If we try to make all depression fit under one way of understanding it I think we end up missing the point. I think when we do that we also probably give the wrong treatments. I think to start with, the treatments need to be more tailored or more individualized to the type of depression that a particular adolescent or even an adult has.

#### Peter Jensen:

You know, that's fascinating. I know we talk here at Mayo Clinic a lot about the need for tailoring and individualized treatments. I know you've been doing some work looking at individual genes and kids' response to depression treatments. What can you tell us about that?

#### Christopher Wall:

We know, for example, that certain people when they're given a type of medication really struggle with that medication either because they have too many side effects or because the medication really doesn't work. Another person can be given the same medication and

the same dose and it works really well for them. The genes that we've started to look at and are available actually for clinical care at Mayo and some other places really look at the way the liver, for example, metabolizes the drug. Those are called the cytochrome P450 enzyme system genes. We know that a lot of people have differences in the way their liver handles medications that are commonly used for depression, like Prozac.

Peter Jensen:

I was going to ask you, when you get these differences, could this mean that people actually have different kinds of depression?

Christopher Wall:

Well, that's the other kind of interesting thing. Not only would a medicine maybe not work as well for someone because their body doesn't handle it as well, but also we've learned that some of these genes are actually in the brain itself and the way the chemistry is handled is actually quite different. So yes, there could be differences in the type of depression that someone has because of the way their brain handles serotonin as a chemical for example.

Peter Jensen:

Absolutely fascinating. You're saying that the genes in the brain or genes in the body's metabolic system, the liver or whatever, could be the place that's causing someone not to respond?

Christopher Wall:

Absolutely. There's pretty compelling evidence that if we can find the right drug for the right type of depression we're going to have a much higher likelihood for helping that person have relief of their symptoms.

Peter Jensen:

Is there anything ready for primetime on this? Is there anything we can do now if someone's not responding or is this all in the research arena?

Christopher Wall:

Right now there are some commercially available tests. We even use some of those here at Mayo Clinic that will give, for example, after a cheek swab you can send the swab in for analysis and then you get a report back that shows, for example, the liver metabolism as well as some of the brain metabolism or response genes that could be causing complications in treatment. That is available and relatively routinely used here clinically.

Peter Jensen:

So when you have a depressed teen, how often do you find you benefitted by using one of those tests?

Christopher Wall:

Well, it kind of depends. If it's someone's first episode of depression we would tend not to order one of those kinds of tests. Instead, if it's a complicated or treatment resistant depression and we have also heard, for example, that they have a hard time with medication side effects we'd be more likely to order one of those tests to help guide our decision making to see if maybe they've just never been on the right medication or maybe they aren't going to respond to a certain class of medications because of their serotonin transporter or serotonin receptor.

Peter Jensen:

Very interesting. We're talking, today, to Dr. Christopher Wall, Assistant Professor of Child Psychiatry and Psychiatry here at Mayo Clinic, who's doing cutting edge work on new treatments for depression in youth. Chris, I've learned so many new acronyms since coming here like TMS, DBS, etcetera. I've been learning that these apply to some of the new, emerging and potentially alternative treatments, maybe where the first treatment for depression wasn't effective. Can you tell us about these cutting edge, new, potentially alternative treatments?

Christopher Wall:

Thanks for that question because it's such an interesting area. The one acronym that you mentioned, TMS, stands for transcranial magnetic stimulation. We even put an R in front of that so it's repetitive TMS meaning that we have a strong magnet that pulses and generates an electromagnetic field. We try to focus that field on a certain part of the brain that we think is implicated in depression that isn't really responding, for example, to a medication. So TMS is actually new and relatively understudied in children, but it was FDA approved for adults in 2009 and is actually being used relatively routinely in clinical practices across the country.

Peter Jensen:

Wow. What are you doing? I know you're on the cutting edge with this, what are you doing with it?

Christopher Wall:

We've done a couple of things. The first is we wanted to see would it be safe and tolerable in adolescents. We found in our first study, which was published in 2011 that sure enough kids could tolerate it. Not only could they tolerate it. We found that five out of the seven that went through our trial were either much or very much improved after a course of treatment.

Peter Jensen:

This was after failing on SSRIs?

Christopher Wall:

Yeah, this is after failing at last two prior medication trials. So, these were kids that had been struggling with depressive symptoms for quite a long time. They had been on medications that weren't working and we tried TMS. We found nice success, good safety, no safety issues in fact and it was very tolerable. So, it was really kind of a great what we call pilot study.

Peter Jensen:

So what are your plans? I mean that's pretty exciting. What's the next step for you with TMS?

Christopher Wall:

As I mentioned, we just are wrapping up a follow-up to that pilot study where not only did we want to see could we replicate those findings in adolescents but we also wanted to make sure that we were focusing it on the precise location called the dorsolateral prefrontal cortex, DLPFC, in order to make sure that we were really optimizing treatment for these kids. But we're working with one of our colleagues in neuroradiology to also look at brain chemistry before and after the treatment. So for kids that are just finishing trial, we measure their brain chemistry using an MRI technique called MRF before they started their treatment and then once again at the end of their treatment to see how the brain chemistry is shifting. I've just been talking with my colleague in neuroradiology and we are quite excited about what we're starting to see. So, we could really be impacting these kids in a way that shows up not just with them and their families saying they're feeling better but also showing the chemistry changes that actually demonstrate that they're actually better.

Peter Jensen:

So what are these chemicals you're looking for and what are you expecting to see, hoping to see or might see?

Christopher Wall:

That's another kind of thing. It's still called research because we're not exactly sure what we're going to find. But in the past when the medications came along like Prozac we really focused on Serotonin, for example. The newer chemistry that we're looking at is, for example, glutamate and gaba and there are different theories about not having enough glutamate or having too much versus not having enough gaba or having too much. So, the idea is with TMS, for an example, you might be able to change levels of glutamate or gaba that you can actually measure with MRF. When you change those levels you might have a good, clinical impact on their depression and their experience in life. Those are the chemicals that I think are probably the hottest of the topics right now in this type of research.

Peter Jensen:

I mentioned the TMS. Now I've learned RTMS. Any other acronyms that are cutting edge potential depression treatments/

Christopher Wall:

Well you also mentioned DBS and that's called deep brain stimulation. That's where they'll actually do neurosurgery and implant a device in the brain to try to treat symptoms that really aren't going away with medications. Obviously, that's a lot more invasive and a lot more risk associated with neurosurgery but we've seen exceptional outcomes for kids and adults that have struggled with very resistant and debilitating Tourette's syndrome, types of dystonias and a variety of other really debilitating conditions. So DBS is fantastic.

I'll throw another acronym at you called TDCS, transcranial direct current stimulation. That's getting a lot of research interest, a lot of articles published in 2012 as well as even this year. That's where you would actually wear a small device and place a couple of small electrodes on your scalp. It's just enough electrical current to create a bit of a tingling sensation on the scalp. But some of the researchers are finding that it seems to be having some impact on mood and anxiety. So, there's a lot more that needs to be studied with this but it's yet another emerging technique. When you start thinking about the brain as being more than just a chemistry organ but an electrical and chemistry organ.

Peter Jensen:

That's very interesting but it reminds me another electrical stimulation device. ECT. Does that still have any kind of role?

Christopher Wall:

I think it does and it obviously gets terrible press. But as a psychiatrist who has worked with folks who no longer eat and they're only a shell of themselves, they just are so sick with depression, ECT is still the gold standard treatment. Because you can take someone over a couple of weeks, using brief ECT episodes and over those couple of weeks they can come back to life for family. When they've started

to recover the family says it's like I've got my dad back or it's like I've got my brother back. It's pretty amazing to see the benefits that ECT still can play in the most resistant and most horrifying episodes of depression. We still do perform it at Mayo Clinic, rarely but in what we feel are life threatening episodes of depression that really haven't responded to anything else. When we do, for example, treat with ECT we have to have three different child and adolescent psychiatrists review the situation to make sure that no one's missing anything that we could try instead because it is pretty invasive treatment when you come down to the idea of having to have anesthesia and recovery process.

Peter Jensen:

Well, just in your discussions you're conveying such a wonderful empathy for these kids. If I still had any teenagers, Chris, I'd be sending them to you.

Male Speaker:

Thank you for listening to Updates from the Mayo Clinic. Thank you to Shire Pharmaceuticals, whose educational grant makes this program possible. For more details on the interviews and conversations in this week's show and many others or to download this segment, go to [ReachMD.com\MayoClinic](https://ReachMD.com/MayoClinic).