**MARK GEORGE:** So one of the real revolutions in understanding the brain over the last few years, is we're starting to understand the different parts of the brain do very different things and that we shouldn't really talk about just the brain, in general. It's actually circuits within the brain.

And so, we've known in other parts of neurology that different faulty circuits can cause a problem in Parkinson's, for a tremor. We know pretty well the circuit and even where the problem is. We can go in and actually rewire or stick a wire in and treat that. We're starting to apply that same concept now and understand more traditional psychiatric illnesses. It's exactly the same thing.

We call a lot of different things depression, and they may be several different sub-diseases, so I call them the depressions. But what seems to be common in many of the is a problem with the part of the brain up here, called the prefrontal cortex, which regulates a deeper part of our brain called the limbic system, or our emotional system.

And when you're healthy, our prefrontal cortex is doing its job all the time. I'm walking down the hall here and I see a colleague who has a bad look on their face, and I start thinking, is that my fault, are they angry at me? Did I do something wrong? And my prefrontal cortex says, no, it's not about you. It's just as likely that they had a bad day or something.

When you're in depression, that prefrontal cortex is not working. You see the sad face on a colleague, you immediately think they're mad at you, and that you've done something wrong, and that you're not worthy. Your prefrontal cortex can't engage in that flexible thinking, that flexible interpretation of the world. And your limbic system, the emotional system just runs rampant. So we think that that cortical, subcortical regulatory loop is just not working when people are depressed, and that if we can get it back working, the depression goes away.

And it's a clever trick, where we just take an electromagnet and we put it on the head. We turn that on and off and it creates a magnetic field that passes unimpeded through hair, if you had it, skin, and skull, and then interacts with the surface of the brain, and creates an electrical current in the brain. So it's actually a way to electrically stimulate brain, but without sticking a wire in. It's just a trick to get through the skull. Now it's an FDA approved treatment. There are over 500 machines sold in the US. We have a couple of machines here at MUSC, and we have very active clinical practice. And it's now FDA approved for treating depression, and it's more and more reimbursed by most of the insurance companies.

So TMS is approved only for unipolar depression. I think it actually works in bipolar depression, but it just hasn't been effectively shown and FDA approved. Unipolar depression, adults over 18, who've typically tried and failed a couple of medications. So, they've tried Prozac. It may have worked and then stopped working, or they couldn't tolerate the side effects. So it's people in that class that have tried talking therapy and medications and they're not getting what they want, or they have side effects that are intolerable.

This trick of being able to get in and manipulate circuits, almost every brain disorder that we can think of, you can think about theoretically, using TMS to make it better. Right now, we're doing studies in bipolar depression in depressed adolescents, and pain syndromes, as well as general treatment of depression. So those are areas where we would love to talk to anybody who is interested.