Ways the Brain Can Heal

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Robert J. Marks:

Greetings. Welcome to Mind Matters News. I'm your dualist host, Robert J. Marks. We are visiting with Dr. Andrew Knox. Dr. Knox is a neurologist at the University of Wisconsin School of Medicine and Public Health. Last time we talked about all of the ways or many of the ways that the brain can break. We included in these strokes, injury to the brain, dementia. We found out, interestingly, dementia can happen sometimes in little kids. We talked about seizure and we talked about functional disorders like non-epileptic seizures and functional gait disorders. So, we're first of all going to talk about how you fix some of these things, be a little bit more positive, and this, I'm sure is what Dr. Knox takes home with him and has warm feelings about when he can help people and talk about some of the ways that we can make people better. So, Dr. Knox, again, welcome.

Andrew Knox:

Yeah, thank you.

Robert J. Marks:

So, let's talk about this. What are some of the tools that we have to fix the brain?

Andrew Knox:

Actually, among the different medical specialties, people often think of neurology as the specialty where we don't have lots of tools to fix things, but that's not really true. There are a number of things that we can do for many, if not most of our patients. I think broadly, maybe you could say a couple different tools We have, and this is going to be different for different disorders, but there are medications that we can use to help address dysfunction in the brain. In the specific field of epilepsy, there are other interventions you can do like surgeries, in some cases. In other cases, dietary changes can be helpful for treating seizures. There are devices that can be used to help address brain problems. Vagal nerve stimulator would be one example that has been around for a long time. And then there are for dysfunction that lies more in the realm of the mind. There are certainly psychologists are helpful too or strategies like cognitive behavioral therapy can address this function.

Robert J. Marks:

Okay. Well, let's talk about some of the medications. I think one of the first ones for depression was Prozac, and I think this is 30 years old or something like that.

Andrew Knox:

Yeah.

Robert J. Marks:

What do these medications do?

Andrew Knox:

So again, there are many different medications for different disorders. If you're thinking specifically of Prozac, that medication is a selective serotonin reuptake inhibitor. So, I think last time we talked about our brain has neurotransmitters, substances that are used to communicate between neurons across the synapse. And these medications basically make those substances more or less available or perhaps more or less active at those synapses. So, it makes a change throughout the whole brain about how it is processing information.

Robert J. Marks:

I see. I also want to talk about the, yeah, because I was on Prozac for a while, and man, it made a big difference. I remember taking Prozac, gosh, this was I guess 30 years ago when it first came out, and my wife made me go to the doctor and he said, "How you doing?" I said, "I'm doing okay." My wife said, "No, he's not doing very well." So, the doctor said, "Well, let's try some Prozac." So, I took some kind of reluctantly, and I remember waking up about a month later and sitting up in bed and going, "Oh my gosh, I'm happy."

Andrew Knox:

Yeah.

Robert J. Marks:

It was a first time for a long time. So, that serotonin, whatever that was, began to flow in my brain and it started to flow and it's been wonderful since. So, that was just an amazing, an amazing medication.

Andrew Knox:

Yeah. That's great. We still definitely use that medication often as a first line treatment for depression. And that's the sort of thing we always hope happens when you use these medications. It doesn't always work out as well as it did for you, unfortunately. And I think that's not totally surprising when you think about how we're using these medications. This is another area, I think where analogies to computers are sort of useful or analogies between computers and brains. Using a medication to change how the brain is working is a little bit like, if you had a computer, let's say you build a computer, computers are built out of billions of transistors, right?

Robert J. Marks:

Yes.

Andrew Knox:

Let's say something was wrong with the transistor that you used to build your computer. So, you have billions of these slightly misfunctioning transistors. If you could, I don't know, let's say do something to your processor that you had that made all of them function a little more like they were supposed to, then it's conceivable that, that might make your computer work better. But it's still a blunt tool. Initially, it seemed preposterous to me that you would expect to be able to give all the transistors a little more electrons or something and expect your computer to work better. But it's kind of work. We're doing a similar thing using medications that work on the brain.

Robert J. Marks:

Interesting. I-

Andrew Knox:

Does that make sense?

Robert J. Marks:

Yeah, it does. What it reminds me of, you always have analogies between what you're learning and stuff you do. Dr. Eggbert, who's the director of the show, and I are working on a project of phased array antennas, and these phased array antennas don't work as well as they could.

Andrew Knox:

Yeah.

Robert J. Marks:

They're depressed. And so, we could go in and we can tune the electronics. We can choose to tune the electronics so that the electronics make it work better. So, I guess that tuning of the electronics is like this Prozac.

Andrew Knox:

Right.

Robert J. Marks:

Very interesting. I think there's analogies all over the place.

Andrew Knox:

Yes. Now, for something like depression, most of us think of depression as just one disorder, but the reality is probably there are many different kinds of brain dysfunction that can lead to depression. So, there may be some patients where the real problem is there is just not enough serotonin around to do the normal sort of signaling, and that's a patient who may respond very well to that medication. But you may have another patient where there is a different neurotransmitter that is out of balance, or perhaps the problem is not a specific neurotransmitter at all. Perhaps the problem lies specifically in the realm of dysfunctional thoughts that this patient has over and over. Maybe they keep thinking, I hate myself, I hate myself, I hate myself, I hate myself. And out of that comes their depression. Those patients, not all of those patients would respond in the same way to a medication like Prozac.

Robert J. Marks:

I see. Because their depression is not due to the flow of serotonin. It is a psychological feedback that keeps feeding on itself. I got it. I got it.

Andrew Knox:

Right. Now, all this becomes more complicated because all these things are related. So, the thought processes are happening in a brain that is built on these physical substrates, and the thoughts you have probably affect how neurons behave. It may affect levels of some of these neurotransmitters. So, it's a sort of large entangled web that you can't, that is difficult to totally understand.

Robert J. Marks:

Okay. One of the statistics I read is that people that take antidepressants are more prone to commit suicide. I thought this was such a stupid statistic because people that are depressed already have this inclination towards suicide, and if the program, and if the medication doesn't work, well, they go ahead with it. It's a terrible thing to advertise.

Andrew Knox:

Yeah. That comes about ... It's on a number of the package inserts of the antidepressants that they may increase risk for suicide.

Robert J. Marks:

But is that really true, Andrew? Or is it that the sample set is actually biased towards suicide in the beginning?

Andrew Knox:

Oh, I think it definitely comes out of the sample set, and some of this just gets down to how adverse effects are reported. So, if you do a clinical trial studying a new antidepressant medication, you've got a group that has a placebo, so is not getting the drug that they think they are sure. And then the group that is getting the true drug, and then you look at how many patients in each of those groups had a particular side effect. So, you could look at suicide and you might say, "Oh, look like six patients who are treated with the medication committed suicide, but only three patients who are treated with a placebo committed suicide."

Robert J. Marks:

Ah, yes.

Andrew Knox:

So, then they would say, "Well, this medication may increase your risk for suicide." But that doesn't show causally that the medication is the reason for you're committing suicide.

Robert J. Marks:

I see.

Andrew Knox:

It's just an association. It may be that everyone was having suicidal ideation and the patients who took the medicine got a little more motivated and more of them acted on those thoughts they were having. And sometimes it can just be natural variation between the two groups too, but you still have to report it if it's there.

Robert J. Marks:

Wow. Interesting. Well, we're talking about ways to fix the brain, and one of them is anti, well is antidepressants, and there's also antiseizure medications. How do those work? Antiseizure medications, how do they figure out where the seizures are coming from and stop them?

Andrew Knox:

Antiseizure medications work in a similar sort of way, really to the antidepressants just acting on different receptors or neurotransmitters. So, many of those medications, the first ones that were created act on a receptor called a GABA receptor or GABA.

Robert J. Marks:

Could you spell that? A-G-A

Andrew Knox:

G-A-B-A.

Robert J. Marks:

GABA. GABA. Okay.

Andrew Knox:

Yep. So, that's usually thought of as the primary inhibitory neurotransmitter in the brain. So, it's neurotransmitter that would make a neuron a little bit less likely to fire off.

Robert J. Marks:

So, some seizures are caused by neurons not firing, is what you're saying? Is that right?

Andrew Knox:

Well, so the idea would be that sometimes if neurons get too excited or they're too likely to fire, then maybe a network of them will produce something like a seizure. And if you give a medication that works, that increases activity, GABA receptors that may make them less likely to fire and you may prevent the seizure from happening. Make sense?

Robert J. Marks:

Yes. Okay. Understood. Well, since we're talking about antiseizure medications, let's talk about epilepsy surgery. I want to tell you a little story. I had a student, a wonderful student, we'll call him David, and David had epilepsy. In fact, he's the one that had a seizure in my office at one time. And that was not fun to look at all. But one of the things about David, he was always positive. He was always happy. He was always, he was a Christian. He was always looking at his happiness and his faith in God. And I tell you, this is a guy that probably will never drive in his life because he has seizures and he has a very limited life.

He's making a good living now as an engineer. But he went in for some epilepsy surgery, and one of the things they did is they cut a flap out of his skull and they placed on his skull an array of sensors that they were doing something with, and it was a total failure. In fact, his brain began to swell up. They had to stop the procedures and sew him back up. So, I guess sometimes those things work, that kind of epilepsy surgery. Tell me about epilepsy surgery and I don't know, do you know what they were trying to do with that array of sensors?

Andrew Knox:

Yeah, I do. Yeah, I'll work up to explaining what they were doing there. So, maybe just some general background. So, many patients with epilepsy will become seizure free on one of the medications they try. In fact, we usually quote, "Two thirds of patients will become totally seizure free on one of their first two appropriately chosen antiseizure medications."

Robert J. Marks:

Wow.

Andrew Knox:

So, those are reasonably good numbers.

Robert J. Marks:

Those are good numbers. My friend David, he tried diet. He tried this operation, everything, nothing worked. So, he was in that one-third.

Andrew Knox:

Yeah. So, he was in that other third. So, we would say they have drug resistant epilepsy. And unfortunately, once you fail two appropriately chosen medications, the chances of responding to other medications gets lower. So, 3 to 10% chance we say for any particular medicine you try. So, like you said, we think about things like dietary options. The ketogenic diet can be helpful for some patients. And then surgical options is the other option. For surgical options, you can think of two broad groups, one group as receptive options, or we would say curative options, things that we think will totally get rid of the seizures. And the other group is palliative options. Things that aren't going to totally get rid of the seizures, but they'll make them happen less often.

Robert J. Marks:

Palliative. What ... I've heard the word. What does it mean?

Andrew Knox:

Palliative means you don't think you're fixing the problem, but you're going to make things better than they were.

Robert J. Marks:

Oh, okay. I tell that with people, "I can't solve your problems, but I can help you enjoy them." So, it's kind of like that.

Andrew Knox:

That is one way to put it.

Robert J. Marks:

Okay. Okay.

Andrew Knox:

That's good. Yeah. So patient receptive surgery, the idea is pretty simple. If you have seizures that only come from one spot in the brain and you can show that that part of the brain is not doing anything else, that's essential. Meaning you wouldn't have terrible problems if it were removed, then you can take that part of the brain out and then the patient's seizures are gone. Okay. So, it's a simple idea, but practically it's difficult to execute that.

Robert J. Marks:

So, I think in David's case, what they were trying to do is they were trying to locate those points of seizure.

Andrew Knox:

Exactly, yep. So, that is the challenge of epilepsy surgery, locating exactly where the seizures come from. We have a variety of different tools for doing that. Different imaging tools, different EEG tools. But even with those tools, we still don't get as definitive an answer as we would like, in many cases.

Robert J. Marks:

I see.

Andrew Knox:

So, in David's case, usually you start by doing some imaging studies like an MRI, functional MRI. You can do a PET scan to look at brain metabolism. You can do a kind of scan called a SPECT scan to look at blood flow at the start of a seizure and then blood flow at other times and see what changes right when the seizure starts.

Robert J. Marks:

Well, that was the interesting thing. He went to the hospital and he says, "All my life, I've been trying to avoid seizures. And I went to the hospital and they told me try to have a seizure." Which was terrible because that's the only way that they could do the localization of his, if he had a seizure.

Andrew Knox:

Yeah. So, that is part of the workup for epilepsy surgery. That's the opposite of what we're usually trying to do.

Robert J. Marks:

Yeah.

Andrew Knox:

So, there are a number of tools that we do. We start out with non-invasive tools, and then sometimes if we need more information, we'll actually record directly from the brain itself, which is I think, what they were doing with David.

Robert J. Marks:

Yes. And unfortunately, yeah, unfortunately it didn't work. So, I guess it works sometimes.

Andrew Knox:

Sometimes you can have edema like that. That's a rare complication, but it can happen in some cases. Thankfully, it's never happened when I've been involved.

Robert J. Marks:

Okay.

Andrew Knox:

Actually, there are two ways you can do that monitoring. You can do it either, like you said, with a grid that you place on the surface of the brain and it records from the brain. Now, we often do stereo EEG, so we pick specific places where we want to record from and then use a robot basically in the operating room to find those exact trajectories that we want, drill small holes in the skull at those locations, and then pass an electrode through into the brain. And it actually turns out that's tolerated much better. So patients, we've done that with a number of patients at this point, and none have certainly had any of those sorts of problems that you were describing with David. Most patients don't even need ibuprofen or Tylenol or anything afterwards. They just are stuck in their hospital bed watching TV and waiting for a seizure to happen.

Robert J. Marks:

That's something incredible. There's no nerves in the brain. Are you familiar at all with Elon Musk's work in Neuralink where he is trying to-

Andrew Knox:

I haven't followed it closely. I've been thinking, as a neurologist, I probably should pay more attention to what he's doing just so I can ask or answer other people's questions.

Robert J. Marks:

Well, I think what he is doing is, I don't think that he wants to link the human brain directly to all of Wikipedia. I'm already direct, I'm already connected with it, the Wikipedia. It's just through my fingers as opposed to my brain.

Andrew Knox:

Right. Yep. In your eyes.

Robert J. Marks:

I only can think of one thing at a time. I mean, when I multiply two three digit numbers, I have to write it down to keep track of my short-term memory and my multiplication tables in order to work it out. So, I don't know what the neural link is going to do in terms of increasing my intelligence. But the place where it seems to be working and working nicely is helping people with, that are paraplegic or have some motor function problems, and they can do things with this Neuralink that they couldn't do before. So anyway, that I think, is promising.

Andrew Knox:

I think so. A number of people are interested in brain machine interfaces, and it is promising, particularly for people who have problems with the normal way that we would interact with the world. So, I think it will do a lot of good for people.

Robert J. Marks:

And I'm just wondering if he or anybody else is looking at these neural links and seeing if they can help do things like diagnose epilepsy?

Andrew Knox:

Yeah, it's using the same basic tools. It's probably ... People are looking at that in different ways. Lots of people in the epilepsy field.

Robert J. Marks:

Okay. We're talking about different ways to fix the brain. We have medications, we have, such as antiseizure medications, antidepressants. We have epilepsy, epilepsy surgery, and another one is devices and the response to neuro stimulation. How do I stimulate my neurons? I think I wake up some morning and I want to stimulate my neurons. So, how do I do that?

Andrew Knox:

Yeah. Yeah. Well, I don't know that you need to use any of the methods we're going to talk about here. Probably going for a run is a reasonable thing.

Robert J. Marks:

Yes, okay.

Andrew Knox:

To try just to get a little stimulation if you're not suffering from these problems. So, there are a variety of different ways neuro stimulation can be done. One of the oldest tools that's been used in the field of epilepsy is the vagal nerve stimulator.

Robert J. Marks:

The bagal nerve. What is that?

Andrew Knox:

The vagal nerve.

Robert J. Marks:

Vagal nerve.

Andrew Knox:

Vagal nerve.

Robert J. Marks:

Not the bagal nerve. Bagel is a type of bread.

Andrew Knox:

Not the bagel nerve.

Robert J. Marks:

Ok. The vagal nerve,

Andrew Knox:

Although the vagal nerve does innervate your stomach, so there might be a relationship there.

Robert J. Marks:

Okay, very good.

Andrew Knox:

Yeah. So, it's a nerve that is responsible for controlling a variety of different autonomic functions, including the stomach.

Robert J. Marks:

What is autonomic? You're using words, and I'm kind of embarrassed I don't know them.

Andrew Knox:

Oh, I'm sorry.

Robert J. Marks:

But I am old enough where I'm no longer embarrassed by asking questions, so.

Andrew Knox:

Yeah, I appreciate the questions.

Robert J. Marks:

Okay.

Andrew Knox:

So, you can sort of divide the nervous system up into two parts. There is the sematic nervous system, so the one that deals with controlling muscles and the senses and that sort of thing. And then there's the autonomic nervous system. That's the one that's responsible for control of your various inner organs or guts and that sort of thing. So yeah, you can think of it as controlling your stomach and your hearts and other organs like that.

Robert J. Marks:

Okay. Thank you. Go ahead then.

Andrew Knox:

Right, so the vagal nerve stimulator, so the vagal, someone discovered that you can attach a device that's sort of like a pacemaker to the vagal nerve in the neck and repeatedly stimulating that nerve for whatever reason seems to make patients have seizures less often.

Robert J. Marks:

Oh.

Andrew Knox:

Not all patients, but many patients. The mechanisms are not well understood, but there's a definite effect there. And subsequently, people have realized that that sort of simulation may be helpful for other disorders too. For example, it can be used for refractory cases of depression.

Robert J. Marks:

Oh, okay.

Andrew Knox:

Yeah. So, that was the first pass of neurostimulation.

Robert J. Marks:

So, I have a cousin that was suffering from a lot of pain, and he went in and they did something with the spine in order to alleviate his pain. And they went in and I guess it's very sensitive to the location. And so they were poking around his ... his problem was with, in his bowel region. And so they were poking around and one of them went directly to his groin and he started jumping up and down and all of the nurses and the doctor said, "What's going on?" And he said, "It's my groin." And they all started laughing. But is that an example of it? Where they do the neurostimulation in the spine in some way?

Andrew Knox:

Yep, yep. That is another good example of neurostimulation. So, for certain pain disorders, spinal stimulation, specifically, can be helpful. I haven't done as much of that myself, but it is another kind of neurostimulation. So, in the field of epilepsy, another option that we consider that's a little more direct would be responsive neurostimulation or RNS. For this device, this device is actually implanted on the underside of the skull, and you leave electrodes in the brain or on the surface of the brain that are attached to the device and the device records brain activity. And then if it detects a pattern that looks like a seizure pattern, it can stimulate those electrodes.

Robert J. Marks:

I see.

Andrew Knox:

The initial idea was this may be helpful because it may interrupt the seizure or prevent it from developing or spreading to other areas, but it turns out there's actually probably also just as much and maybe more benefit that comes just from giving periodic stimulation to that area of the brain that's irritable and is producing seizures.

Robert J. Marks:

So, this sounds like a device that's wearable, is that right?

Andrew Knox:

So, this is not wearable because it's implanted into the skull itself.

Robert J. Marks:

Oh, okay. Well, yes.

Andrew Knox:

So, you keep it with you all the time, but you're not, well, I guess you're wearing it instead.

Robert J. Marks:

It depends on your definition of wearing, I suppose.

Andrew Knox:

Right, right.

Robert J. Marks:

Okay. Yes. Understood.

Andrew Knox:

Yeah. So yep, you keep it with you all time. And then there's a way to load information from the device to a computer so your epilepsy doctor can look at the patterns that are happening, determine how often seizures are happening, and then decide whether we need to tweak how the device is detecting seizures or stimulating to prevent them.

Robert J. Marks:

I see. Is this a common thing? I don't know if I know anybody that has these things with a transplant. I don't.

Andrew Knox:

Yeah.

Robert J. Marks:

You wouldn't call it a transplant, you would call it-

Andrew Knox:

I wouldn't call it a transplant. Right. Because it didn't come from another person. Implants. I think you would say.

Robert J. Marks:

Implants. Implants, that's a word I'm looking for.

Andrew Knox:

Yeah. It's usually not the first thing we go to. This would be used in patients who do have seizures coming from one area of the brain, but there might be some reason you wouldn't want to remove that area. Perhaps it's an important motor area or an important language area. It also gets used occasionally if you have seizures that are coming from two different places. Say you have seizures that are coming from both of your temporal lobes, we know that you can't remove both of your temporal lobes because if you do, you'll lose the ability to form new memories. So, the device can be used as a way in that scenario to help control the patient's seizures.

Robert J. Marks:

But before you use this, you have to know the source of the seizures. Is that right?

Andrew Knox:

That's correct. Yep.

Robert J. Marks:

Okay.

Andrew Knox:

So, a lot of time and energy and effort is spent doing our best to pin down exactly where the seizures come from.

Robert J. Marks:

Okay. How to fix the brain. Medications, epilepsy surgery, neurostimulation devices. And the last thing I want to talk about, and this is a good segue into our next topic that we're going to do in the next podcast, is cognitive behavioral therapy. Tell me about that.

Andrew Knox:

Right. So, cognitive behavioral therapy lies in the domain of the mind or the realm of psychology. The idea of cognitive behavioral therapy is if you have a disorder that's coming from pathologic thought processes, cognitive behavioral therapy involves meeting with a psychologist to better understand what kinds of thoughts you're having, what particular thoughts may not be beneficial or maybe causing the dysfunction, and then coming up with ways to change those thought patterns. So, one example might be if someone had say, an eating disorder, because every time they looked at those, themselves, they thought, I look terrible, I'm horrible. I look ugly. The goal would be to get an idea of what specific thoughts are involved in that cycle.

Robert J. Marks:

Yes.

Andrew Knox:

And then you would try to learn to replace those thoughts every time they happened with something else. Like, no, I know that's not true.

Robert J. Marks:

In fact, that that's a common symptom of depression. You think that you're no good, that the whole world's better than you are, and I guess that just feeds back in itself and it makes you feel worse. But you're saying that this can be treated with therapy then?

Andrew Knox:

Right. Exactly. So, for many disorders, that is considered the gold standard for treating them. Particularly, I'm thinking back to functional disorders that we've discussed already.

Robert J. Marks:

Yes.

Andrew Knox:

That is the most effective thing we have to cure some of those disorders. Now, obviously, that's not going to cure everything. Your cure needs to be targeted to what the problem is. So, you probably wouldn't cure epileptic seizures with cognitive behavioral therapy. That wouldn't be expected to work at all.

Robert J. Marks:

Of course.

Andrew Knox:

But for many disorders, it can be beneficial or even the gold standard treatment.

Robert J. Marks:

I have a good friend, and you probably maybe know him professionally. I don't know if he's a good friend. He certainly an acquaintance, JP Morland from Viola University, one of the greatest living Christian philosophers. And he suffered from incredible depression. And he wrote a book about it called, Finding Quiet. I would recommend it to anybody who is suffering from depression that doesn't want to go to a therapist that maybe wants to self-treat, but it's called, Finding Quiet. And one of the things that, well, he says, "First of all, you got to involve yourself." He's a Christian. So he says, "Involve yourself in prayer, but go to the psychiatrist and get the medication. Go to the psychologist."

But one of the things he found very useful is anytime he had a depressing thought, he always gave it a name like Frank. And so he had this depressing thought and a depressing thought that he was no good, and he would talk to Frank as opposed to pound it down inside of him. And I thought this was really ingenious. He said, "Hi Frank, boy, you're back again. I didn't want you back, but here you are. You know what? I don't have time for you now, but maybe later, go away." And so he dealt with it in that specific fashion. And I'm sure that this is part of this therapy that people go through for depression, doing things like that and going through these mental exercises in order to break that loop, that feedback loop that makes them more depressing.

Andrew Knox:

The goal of therapy is always to give the patient techniques that they use to address those problems. So, you always think of it as a time, not when you're trying to teach someone how to, those sorts of strategies to order their mental life as opposed to just the thing itself that helps being there in therapy.

Robert J. Marks:

Wonderful. Wonderful. Oh, look. Thank you, Andrew. We've been talking to Dr. Andrew Knox, and we're going to continue this. And our next podcast is going to be on a really fascinating topic that is the mind brain problem, whether the mind is part of the emergence of the brain, or whether there's something going on external to the brain, which we can call the mind. Dr. Knox is a pediatric neurologist at the

University of Wisconsin School of Medicine and Public Health, and we thank him for his time. And so until next time, be of good cheer.

Announcer:

This has been, Mind Matters News, with your host Robert J. Marks. Explore more at mindmatters.ai. That's mindmatters.ai. Mind Matters News, is directed and edited by Austin Eggbert. The opinions expressed on this program are solely those of the speakers.