Terri Murray: Engineering Ways to Treat Brain Disorders – Season 1, Episode 2

Amy: You're listening to “Beyond 1894,” a podcast where we hear from Louisiana Tech University scholars, innovators, and professionals on their personal journeys and the impact they're making in the world around them. I'm your host, Amy Bell, and my co-host is Teddy Allen.

Amy: In this episode, we hear from Dr. Terri Murray. She is an Associate Professor of biomedical engineering in the College of Engineering and Science here at Louisiana Tech University. As the director of the Integrated Neuroscience and Imaging Laboratory, she is committed to exploring solutions and developing therapies for brain injuries, neurological disorders, and neuro cardiovascular diseases. In the interview, we talked about how she stumbled upon biomedical engineering, how she began studying the brain, and the projects she is working on currently.

Terri: We know something changes in the brain before a seizure, but being able to predict it is a lot more difficult. And to have something that's accurate enough and give somebody enough time to react is important because people like my brother-in-law could drive if they had enough warning, you know, if it were possible to have a 20-minute warning that they were gonna get a seizure. If you were driving, you can pull the car over and park and wait for the seizure to end and then after you felt better you could get in your car and you could drive.

Amy: Honestly, I was pretty swept away by the science she explained to me. Like, for example, what happens in the brain when someone is having a seizure? I thought she did a really good job of explaining that.

Teddy: She explains things in a way you can understand them. This is probably the only podcast, at least so far, that's mentioned rats, gerbils, horned toads, and newts that I can think of. She touched all the bases. When she was little, it’s wonderful hearing about her exploring and she's always had this passion and she didn't realize what it was hooked on to, didn't even know what biomedical engineering was. After she saw a TV show one night and a paraplegic was walking because of some wires that men and women had put in his legs and she jumped off the couch and said “I want to do *that*.” And so she went and figured out what “*that*” was. And it turned out to be biomedical engineering.

Teddy: She loves it. You can tell by listening to her talk, that's what makes this podcast so good, in my opinion, is it’s somebody who found out a little later than she wanted to maybe perhaps, what she wanted to do, and she had been successful doing some other things. But when she saw that, she said “Yep, that's me. So, I'm gonna go back to college, while my kids are in high school,” and, you know, got her doctorate, and now she's helping people, right and

left. The government federal grants has given the lab hundreds of thousands of dollars for this worthy research that's gonna, well, benefit a bunch of people. So, thanks, Dr. Terri.

Amy: Is there anyone in your life that is going to benefit from this research?

Teddy: I know a couple people who could have benefited from it, who suffered traumatic, you know, injuries, and the research at that time was not to the point where it is now where they could be helped**.** And so, I am thrilled that this money has been invested in this worthy lab, and that Dr. Murray's over there knee deep in it working as hard as she can with her fellow scientist to help somebody out that, you know... and it could be that you or I need help one day in that regard. So it's the least understood part of the body I guess, the brain, certainly by me.

Amy and Teddy: [Laughter]

Amy: How ironic that you have to understand the brain with your brain.

Teddy: Right. That's a... tough break for a guy walking in my shoes, but... so I'm glad Terri's out front.

Amy: So let's play the interview now. And I hope everyone enjoys it.

[Start of Interview]

Amy: As a kid, what did you dream of being as an adult?

Terri: Oh, I dreamed of all kinds of things, but mostly an explorer or a scientist.

Amy: Okay, did you have an idea of, like, what you wanted to explore or what kind of scientist?

Terri: Not at all, but I was enamored with the natural world when I was a kid. I was always picking up rocks and dead bugs and things and going to my books and trying to find out what they were and what they were made of and how they worked.

Amy: That's awesome. Did you live in a pretty, like, green area?

Terri: I did! There was a forest preserve in my backyard, and so that allowed me to go in and see all kinds of birds and wild animals, and... *[pauses]*

Amy: It sounds like you had a really cool, fun childhood.

Terri: I did. You know, we would collect turtles and frogs and things from the swamp that was just, oh, about a half a mile away. Just long enough to walk to and back and think it was very, very far away as a child. And we would bring them to our homes, care for them for the summer

and then return them to the swamp because we were told that they had to burrow down in the mud and that was fascinating. I didn't have any clue as to how they breathed down there as a child, but we dutifully returned them to the swamp right about the time school started so that they could burrow down in and we could get them the next summer.

Amy: Did you have a favorite thing to collect?

Terri: No, I was all about collecting something new and different. I went in with two of my other friends. We took our babysitting money and started buying exotic pets at the pet store like newts and chameleons and horned toads and things like that and gerbils.

Amy and Terri: [Laughter]

Terri: Course, our mothers were not very happy. We figured out a way to appease them by having the animals at one person's house for three weeks, and then the next one for three, and the next one. So it was six weeks off and three weeks on and that was tolerable for our mothers.

Amy: You shared custody!

Terri: [while laughing] We had shared custody!

Amy and Terri: [Laughter]

Amy: That's awesome. So... okay, when you got older, when you were in high school, in college, did you have a clear-cut path? Did you know exactly what you wanted to do?

Terri: Oh, I wish I could say “yes” to that, but... I did want to become an engineer. But when I was in high school, it was the late 1960s and women didn't become engineers.

Amy and Terri: [Laughter]

Terri: And so, I was told to learn how to type and be a secretary and... now I was very miserable at that.

Amy: Did you try that?

Terri: I did. I didn't try it for very long. The only job I was ever fired from was typing for a newspaper and... *mercifully*, three weeks later, the guy came in and said “This isn't working out.” I'm like “Oh, thank you. Thank you.”

Amy: So how did you get interested in biomedical engineering?

Terri: Well, it would be a few years. By then I was married, and I helped my husband start a number of businesses in manufacturing and the food service business. And I did that for quite a

while. I did go to community college and I took marketing and sales and management and worked my way into a couple of big companies and did that. I was quite successful at it, but it wasn't my passion. And when my children were in high school, I was determined to get back to college and study something I was interested in, possibly geology, learning about the natural world, or engineering. Although, by then I had decided I didn't really want to build bridges. I didn't want to build sewer treatment plants. I didn't want to run a factory and so I wasn't quite sure what I would do as an engineer. But it was still very appealing.

Terri: I like designing and building things, and I had discovered that I was actually pretty good in 3D space and thinking things through my head in space and time. And so I realized I would probably be a good engineer, but I just lacked a passion for doing something with it. Until I found a program called *Scientific American Frontiers*. It was on PBS, and every week they had some new thing that scientists or engineers invented and, you know, it was revolutionary... revolutionizing, you know, fields. And I saw some engineers and scientists put wires into a paraplegic's legs. And that person who hadn't walked since a motorcycle accident got up and, with the help of a walker, walked on his own. And I got up from the sofa, I looked at my husband, and I said "I want to do that!"

Amy: Wow, yeah.

Terri: And I found my passion. I still had no idea that there was a field called biomedical engineering. I'd been out of school for years and when I first went to college, that wasn't an option. And so I looked at all the classes that I thought I would need to have, you know, biology and physics and materials and engineering and things like that, and stumbled on this field that had all of that called biomedical engineering. And so that's what I ended up going into, as a middle aged woman, with kids in high school going to college.

Amy: Wow, yeah. So what was that like for you?

Terri: It was strange being in school with students that were the age of my children, and we didn't have a lot in common. I didn't live in a dorm. I drove home and went back and cooked dinner with my husband. So it was a very different experience where I ended up being able to connect with students and quite easily was getting involved in student organizations.

Amy: Okay, yeah!

Terri: And so I got involved with the Biomedical Engineering Society student chapter and then eventually the Honor Society. I also was on the Academic Senate for graduate students when I went into graduate school. And that gave us common purpose and common things to talk about and then I found myself getting invited out for beers afterwards and it was a lot of fun.

Amy: Let’s take a quick break to learn more about the Biomedical Engineering Program in the College of Engineering and Science.
[Biomedical Engineering Commercial]

Louisiana Tech offered one of the first majors in biomedical engineering to train graduates to work in the pharmaceutical industry, create medical devices, and even teach NASA astronauts to wear their spacesuits properly.

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Amy: And now let’s get back to the interview with Dr. Terri Murray.

Amy: Whenever you're studying biomedical engineering, was there a certain topic that really excited you and you thought, “Oh, I want to know more about this,” or “I want to research this.”

Terri: All of them. [laughter] It was just an amazing program, I would have to say that the materials captivated my interest and also all of the biology, particularly physiology, like how, how does the body work together? How does the liver get rid of the garbage in the body and the kidneys? And then particularly how the brain works. And that's what I ended up getting into in my research field was when I started learning how the brain works, and all the different types of cells that are there and the things that are on those cells that make each cell unique, and how they need to all work together as a network.

Amy: What do you mean by cells on top of cells?

Terri: Well, it's like if you think about a shopping district in a downtown area, and then the streets and the traffic lights and everything in all of the infrastructure to keep all of those businesses going like the electricity and the water lines, and the plumbing and everything. There's an analogy that you could make for every one of those parts of the brain. You can go back to how a city works. And you need all of those. You need good blood circulation. If you don't, you've got a stroke, and then bad things happen. The police, the police keep order. And there's an immune system in the brain that's unique to the brain that helps keep things in order. They do it chemically and not with, you know, guns and billy clubs and tasers. It's not quite that aggressive! But yeah, they actively keep the brain healthy, or try to. And then I got into that age group where my grandparents and aunts and uncles started getting sick and there was Alzheimer’s disease and Parkinson's and cancer and things like that. And then I really got interested in learning about how to study the brain to see if we could learn more about it, to find better ways to treat these disorders to either cure them, or at least treat them better. So people could be more functional.

Amy: Yeah. I remember, before this interview, when we were talking on the phone, you told me that your brother-in-law has Alzheimer's, or no, no, no, he had epilepsy, I'm sorry.

Terri: Yes, my brother-in-law had epilepsy. And he got it as an adult, it was very strange. He hadn't had a seizure until he was probably 50 years old.

Amy: Wow.

Terri: But he was working with chemicals. And to have epilepsy, if you've had one seizure, you don't have epilepsy, you've had a seizure. And if it never happens again, you just had a seizure. And they could be brought on by a number of different things: a blow to the head, chemical exposure, drugs, all kinds of things. But to have recurrent seizures, that's epilepsy. And he developed recurrent seizures, and he had to take leave of absence from his job and when he was finally able to go back because the medicine was controlling his seizures, he still couldn't drive. My sister had to drive him to work. And it's a terribly disruptive disease. And when it strikes young, it can affect a child's ability to learn. And, you know, certainly it affects memory at any age. And that inability to learn consistently is very disruptive to young children. Some of them are, you know, developmentally delayed because of that. And adults suffer from memory loss, sometimes emotional issues in that, because the brain is somewhat damaged, even though the seizures only last for a few seconds usually. They usually end on their own and the person either gets up and does what they've been doing, if it was a mild seizure, or sometimes there's a bit of a recovery afterwards. But the seizure's over and you would think that they would be fine. And we're finding out that they're not.

Amy: So, it's the damage of the seizure?

Terri: The brain, we believe, and this is one of the things we're studying with the Neuro NEM is that the brain rewires a little bit. The brain has trillions of cells and they're all connected in one way or another. Not all together, but connected in neighborhoods.

Amy: Like electrical lines?

Terri: Like electrical lines, or like a city that has neighborhoods that do different things like a theater district and a dining district and a hospital district and so forth. But the connections between those different centers can change. And we think that that's what propagates the seizures, for one, but it also seems to be interfering with cognition, memory, and sometimes even emotions. And we're really just scratching the surface now, because it's only been recently, you know, in the last decade that we've had the tools to go in and record deep in the brain of human beings. And that we've had noninvasive ways to image their brains to see them functioning in time.

Terri: I actually work with rats, so I don't get to work with the "people" side. My role in the project is to work with rats and use them as a model. So we actually give rats epilepsy by starting out

with one big long seizure, and then after that big long seizure, they start having seizures on their own. So, the first one is initiated with a combination of some drugs and then a few weeks later, they start having seizures spontaneously, no extra drugs, just on their own.

Amy: So, the drugs that you give them initially is what triggers epilepsy?

Terri: It triggers a very long episode of muscle convulsions. And then, generally they rest for a while because they're tired, you know, and everything seems fine for a couple of weeks or more, and then they start developing those little convulsive motor twitches, and that sort of thing that's very characteristic of epilepsy. Of course, not everybody with epilepsy has motor contractions, and that some people with epilepsy will just lose part of their consciousness, and they'll just stare off into space, or they'll become confused. And so there's actually many different kinds of epilepsies.

Amy: And that's considered a seizure?

Terri: And that is still a seizure, because a seizure is when the brain is not functioning correctly.

Amy: Oh, okay.
Terri: As a matter of fact, it seems that it's overactive, it's over connected. Everything's connected instead of each area doing its own particular job. It's just all active at the same time in the same frequency.

Amy: And so using your metaphor, the community metaphor, is it kind of like if all of the stop lights were green, and there's a lot of traffic?

Terri: It would be like all of the stop lights flashing green and red and green and red, and nobody can go anywhere because that's not green enough to go. Yeah, it's not green long enough, and it's just like, everything comes to a standstill, the city no longer functions.

Amy: It's chaos.

Terri: It's chaos, exactly. As a matter of fact, chaos theory has been put to use by Dr. Leon Iasemidis, who's the principal investigator of the NeuroNEM project. He's the one who initiated all of this, and he recruited people called co-P.I.s, P.I. for "principal investigator." I am a co-P.I. and I'm one of about five of them in the project and we each manage one aspect of that project, and coordinate the efforts of other researchers as well that are in the project. So we've got quite a few at three different institutions. The institutions are the University of Alabama at Birmingham, and the University of Arkansas for Medical Sciences in Little Rock, Arkansas. And so those two have medical centers and Epilepsy Monitoring units and treatment for epileptic patients. So they are the clinical side of this project. And then I'm managing part of the animal research that's going on.

Amy: We're going to take a quick break to learn about the Parkinson Resource Center here at Louisiana Tech University.

[Parkinson's Commercial]

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Amy: And now we are back with Dr. Terri Murray. She is an Associate Professor of biomedical engineering and she is the director of the Integrated Neuroscience and Imaging Laboratory.

Amy: So how did you get recruited onto the project?

Terri: I've known Dr. Iasemidis a very long time. We met in graduate school when he was in Arizona State University and I was a student there.

Terri: I had an idea for a project. I had a fellowship from the National Science Foundation, and I had my own project and was having a very difficult time getting any of the faculty members to let me do my project. They wanted me working on their projects. And Dr. Iasemidis was the only one who would let me work independently on my project. And we would just check in periodically, and he would keep me on track with things like, you know, the administrative type things and also asking me hard questions that I needed to think about. Even though he wasn't an expert in what it was I was doing, he had an uncanny knack to ask questions. "Well, if this doesn't work, then what is your plan for the next step?" And, of course, I had everything all laid out as if it was all going to work perfectly, and it didn't.

Amy and Terri: [Laughter]

Terri: And so he was right. And I thank him for that, because somewhere along the line, I developed "Plan B" in my research, and "Plan B" is what actually had the greatest amount of success.

Terri: I ended up researching something called a neurotransmitter receptor. So one of those parts in the brain that recognizes, we call them signals, when neurons talk to each other, we sometimes call it signals, you know, kind of like you're doing some radio transmitter and a receiver, sending a signal. Because in the brain, it is electrochemical. So there is some electricity, so it's a signal. I studied nicotinic acetylcholine receptors, which is a long word for the receptor that recognizes a neurotransmitter called acetylcholine. But how it got the name "nicotinic" is that researchers realized that they were sensitive to nicotine. So they could take the signal from nicotine as well as from acetylcholine, these two different chemicals, and make the brain function just as well.

Terri: And those two molecules really don't look a lot like each other. And molecules that activate receptors generally are like a lock in a key. So the molecules, the "key," and the receptors, the "lock," and only certain keys will fit into the lock. So I thought it was really interesting that these two keys didn't really look too much alike, but they had parts of them that were almost identical to each other. And it was those parts that interacted with the receptor that made all the difference. So you can cut little extra grooves in your key and the key will still work. You just have to leave the important parts in the exact same position or your key won't work in the lock. And that's how nicotine and acetylcholine work in this receptor.

Terri: So that was really interesting because then that's useful for studying depression, addiction, Alzheimer's disease, which is why I was interested in it, and a number of other disorders, Parkinson's, and that when there's malfunctioning of those receptors or that system, then you can get that wide range of disorders.

Amy: You were telling me how you got involved with Neuro-NEM. So, then what happens when you got to Tech?

Terri: Well, I opened my lab up and I started doing work on imaging in the brain using tiny little glass lenses that are implanted in mouse brain. And it doesn't hurt the mouse because, guess what? There are no pain receptors inside the brain. So, we could keep these mice alive and study them periodically and look at the brains after a stroke, after traumatic brain injury. So those are other things that I work on in addition to epilepsy. And so I was doing that and the Chair of the Department of Biomedical Engineering, it's actually a program but anyway, the chair said that they wanted to recruit a high powered faculty member, they had an endowed professorship available. And that chair was also at Arizona State University when I was a grad student. And he had come here because this is where he had gotten his PhD. And he wanted to build up the biomedical engineering program like he had done at Arizona State. And so, he was excited about having this money to hire somebody who was a very strong researcher, a lot of grants, a lot of papers, a big impact. And he mentioned that he wanted to recruit Dr. Iasemidis. And I'm like "Okay, well, I like that idea." It would be weird. He was my advisor. Now, he would be a colleague, but I did it very gladly. And fortunately, he said "yes," and great things have happened since.

Amy: Wow. Yeah. And so you've been a part of his Neuro-NEM team. And so in the beginning of this conversation, you were telling us a little bit about your role in the project, but can you expand on it a little bit more?

Terri: Sure. So, we have some people that are primarily doing outreach. The National Science Foundation is very interested in educating our future workforce in science and math. And so we have Katie Evans, who's Chair of the math program, is highly involved in that, and then we've had some other faculty come and go that have been involved in outreach such as our summer program, our research experience for undergraduates, where we take five undergraduates here at Louisiana Tech and put them into our labs to work for the summer and do a real research project and present a poster on their work. And that, it gives them a lot of experience and lets them know if that's something they want to pursue, you know, research as opposed to working for industry or sales or something like that.

Terri: Then we also have five other research experiences for undergrads at the other two institutions. So it's split. One year, three will go to Birmingham and two will go to Little Rock, and then it'll switch the next year, in that. So we give 10 undergrads an experience that they'll never forget. Usually, sometimes really [a] career changing experience for them. Then we've got the work with cells and with animals. So well, you can't do everything you want to do with people. There are some ethics involved. You can't give a person who's healthy, you cannot give them epilepsy. That’s not allowed. You can't cut their head open and start putting little lenses in and things like that. That's not approved. So we use animals, and we also use brain cells grown in dishes. And so Dr. Mark DeCoster is in charge of that. He can take brain cells from rats and grow them in dishes and do various things with them. We've also measured some of those neurotransmitters being released from some of those cells. We've developed some biosensors with another Louisiana Tech investigator, Dr. Prabhu Arumugam, and he's in mechanical engineering. And he develops biosensors, and we were able to put some of his biosensors into dishes of cells and measure the glutamate. Then later, we were able to measure other neurochemicals in rats.

Terri: So my work is with rats. And so we are looking at the electrical activity in the brains of eight rats at any one time over the course of about three months. Some of them have epilepsy, and some of them don't. And Dr. Iasemidis lab is looking at and interpreting those electrical signals to try and develop a better way to predict seizures. What happens in the brain --- we know something changes in the brain before a seizure, but being able to predict it is a lot more difficult. And to have something that's accurate enough and give somebody enough time to react is important because people like my brother-in-law could drive if they had enough warning, you know, if it were possible to have a 20-minute warning that they were gonna get a seizure. Well, if you were driving, you can pull the car over and park and wait for the seizure to end and then after you felt better you could get in your car and you could drive.
So that's one of the things that I do is I implant the electrodes into the brain and monitor the rats.

Terri: And then another project that I'm working on is with Dr. Arumugam, looking at sensing neurochemicals, the two main ones in the brain. One is glutamate. That's what excites the cells. We call it “excitatory.” That excites the brain cells to send signals, to send their neurochemical signals out. And then GABA is another kind of neurochemical that puts the brakes on it. So, you know, it's like having that roller coaster. You know, you get a lot of glutamate and you go “Whee!” and you can go up and down the hills and GABA is like “Oh my gosh, we're going too fast, we're gonna crash! No!” and it puts the brakes on. And so we're looking at GABA and glutamate, and we were lucky enough to get recordings of these before, during, and after seizures. And we just wrote that up in a paper for one of the nature journals, *Scientific Reports*, and it's starting to get a lot of interest. And we want to do more of that, and see if that's also a way that we could look at what's really driving the seizures. Is it too much gas? You know, too much glutamate? Or is it not enough brakes? Not enough GABA? And so that's what we're going to be looking at next is that system of slow and go, you know, when it gets out of hand, you know, is it too much glutamate? Or is it just like, we don't have GABA? We don't have the brakes.

Amy: Yeah. And so you're basically trying to figure out what's causing the chaos?

Terri: Causing the chaos. Because when we know what causes it, then we can go in more intelligently with drugs or maybe electrical stimulation, like a deep brain stimulator for Parkinson's. We could use something like that. But we have to know what to stimulate or, what to inhibit with a drug or what to excite in order to keep the balance. And as anybody that looks at these recordings of the electrical signals going up and down, it does look like chaos.

Amy: Wow. Yeah. That's really fascinating, though, and it seems really rewarding too because you really are helping people. Where are you hoping that the fields of biomedical engineering will go in the future?

Terri: I'm hoping that we can use the tools that we develop in this field to be able to better diagnose some of these “syndromes,” these connected “Spectrum Disorders.” I guess spectrum would be the better term to use, such as autism. When they say “autism spectrum,” it's actually a wide range of different pathologies that all have sort of the same symptoms. The same thing with dementias. Not all dementias are Alzheimer's disease and Alzheimer's disease I believe is pretty much a spectrum disorder. I mean you have people that have amyloid plaques in their brain and, you know, they found that in an autopsy, and the person never had an episode of forgetting or being confused, and yet somebody else who clearly had the symptoms of Alzheimer's disease has the same distribution of amyloid plaques. I think that we can do a better job of developing tools that will look at these biological markers or biomarkers and help us better understand what somebody has because it's just about impossible to treat anything but the symptoms if you don't know what's causing it.

Amy: Well, thank you again for being on here! It was a pleasure!

Terri: Amy, I've really enjoyed it too. Thank you so much for the opportunity to talk about the work in my lab and my colleagues' work.

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Go Dogs, and Ever Loyal Be.

[Outro]

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