BTB S3 Episode 9 Andres Lozano Transcript

BTB
Welcome to behind the breakthrough the podcast, all about groundbreaking medical research and the people behind it at Toronto university health network, Canada's largest research and teaching hospital. I'm your host, Christian Coté and on the podcast today, we're so pleased to be talking with UHN neurosurgeon, Dr. Andres Lozano, an award-winning senior scientist, at UHN's Krembil research institute. Dr Lozano is a pioneer in the clinical use of deep brain stimulation to treat movement disorders such as Parkinson's and a world leading researcher investigating DBS to treat other diseases of the brain, such as Alzheimer's and depression. Dr Lozano is the most cited neurosurgeon on the planet in the field of deep brain stimulation. Dr. Andreas Lozano, welcome to behind the breakthrough.

Dr. Andres Lozano
Thank you very much Christian, pleasure to be here.

BTB
Let's start with the origins of deep brain stimulation and what it is?

Dr. Andres Lozano
Well, deep brain stimulation is a method where electrodes are placed within the brain to very precise areas of the brain to stimulate brain circuits. And in doing this, we can actually drive the activity of circuits that are underperforming like memory circuits in Alzheimer's. Or we can also suppress the activity of circuits that are overactive. These electrodes are implanted permanently. They're hooked up to a pacemaker that is worn very much like a cardiac pacemaker under the skin, on the chest and with a remote control, we can actually adjust the activity of stimulation so that we can actually decide how much electricity to deliver to any part of the brain.

BTB
And where did it come from, the idea of, you know, such an invasive type of surgery to basically treat people where did it come from?

Dr. Andres Lozano
Depends how far you want to go back to the roman times on electric eels, where electric eels are placed on the skull, and they were able to elicit interesting phenomenon. So electricity has been known to activate the brain and over the course of time, experiments about 100 years ago using animals, it was known that if you stimulate the brain, you could provoke movements or you could change the behaviour of animals. And so it was logical to use the same technique in humans. And in fact, in Canada, dr. Penfield dr. Wilder Penfield, one of the pioneers of neurosurgery in Canada, used electrical stimulation to map out areas of the brain and spine to try to reveal what areas of the brain were doing using electricity to activate those areas and looking at what the electrical stimulation of those areas did.

BTB
And to me, what's amazing, having watched one of your surgeries, andreas. What's amazing about a DBS procedure is it involves cutting open the top of the skull and

performing the procedure entirely while the patients are fully awake. So I haven't done it justice. Do you mind walking us through, you know, what do you do in a DBS surgery?

Dr. Andres Lozano
Well, that's indeed what we do. We anesthetize the scalp and the skull and the brain does not feel pain, and so we're able to go without causing any pain into the brain to put electrodes in the brain very much the size of a strand of spaghetti into the brain, deep into the brain. And we're able to probe and stimulate the brain as we go along until we elicit what we're looking for. In some cases, we're stimulating and producing a movement of the arm or leg or fingers. In other cases, we are producing a vision, and it's still in other cases, we can produce a sensation. We can produce even a memory. And so depending on where we are in the brain, we can produce a variety of findings. And this is essential to have the patients awake because the patients then tell us what they feel, what they experience as we are applying electrical stimulation to their brain.

BTB
So DBS has been approved as a treatment for patients with Parkinson’s since the late 90s, is my understanding. Do you understand or have a sense of why it's been so successful?

Dr. Andres Lozano
Well, in patients with Parkinson’s disease, they have difficulty moving or they have tremor. And as soon as you turn on the stimulation and you apply electrical stimulation to the abnormal activity in the brain, the abnormal circuits. There's an immediate improvement. And so you can see it immediately. And this is a very striking thing. So you have someone who's shaking uncontrollably or someone who can't walk and you turn on the stimulation and immediately they're able to go back to normal where the shaking stops instantly or they're able to walk. And so it is a very gratifying, a very visual experience to see. And so in the case of movement disorders like Parkinson’s disease and tremor, DBS is well established and over 200,000 patients worldwide have received DBS. We've done over a thousand of these procedures in Toronto. And so it's a well-established technique.
With the success of deep brain stimulation with Parkinson’s disease and other types of movement problems. We wondered whether we could apply the same techniques to other circuits in the brain to control other problems. That and this is where the possibility of using deep brain stimulation, not just in circuits that control movement, that circuits that control your mood or circuits that control your memory or circuits that control your appetite came in. And this is where the experimental nature of our work comes in, where we are applying deep brain stimulation not only to well-established circuits that we know it works, but we're also jumping into the unknown and into the unexplored and applying DBS to areas of brain where no one has ever stimulated before.

BTB
And have I got this right, your entree into investigating the potential of DBS for Alzheimer’s started back in 2008 with sort of a serendipitous discovery?

Dr. Andres Lozano
That’s exactly the case. We were asked to consider treating a patient with morbid obesity, a man who had tried every diet, who had tried surgery for his obesity and yet was, you know, over 400 pounds. And we wondered whether it was possible to stimulate areas of the brain that are responsible for appetite. So we wondered whether one could

stimulate an area of the brain in a human being and see whether that would diminish their desire to eat. And could this be used in the long term to control someone's weight? So we presented this to our ethical committee at the hospital, and they thought this was extremely controversial. They assembled a panel of 10 world experts. I had to present the, the data and the proposal of the experiment to them. This took about half an hour to present the background and rationale. They then asked me to step out of the room, and then they deliberated. And when I came back into the room, they said, okay, there are six votes for and four against. So on the basis of that, I was allowed to apply deep brain stimulation in a single patient with morbid obesity to see whether that would be helpful to treat their obesity.

BTB
No pressure.

Dr. Andres Lozano
No pressure.

(BTB laughing)

BTB
So it was during that surgery that you discovered something besides the fact that perhaps DBS can help with controlling weight, correct.?

Dr. Andres Lozano
That's right. And so in the course of the surgery, we are probing the brain. We are stimulating millimeter by millimeter to see if we can find an area where we can suppress appetite. So we would ask the patient, you know, how hungry are you on a scale from zero to 10? So his answer was always nine and a half out of 10, and we were looking for a spot in the brain where we could turn on the electricity and reduce the appetite from nine and a half down to something much slower. But we did not really find that, unfortunately, instead as soon as we turned on the stimulation where we thought we needed to go, he described a vivid memory. He described that he felt he was 20 years old and he was with his girlfriend walking through a field. So we were completely flabbergasted by this completely taken off guard and surprised we turned it off. The memory went away immediately. Turn it back on, the memory comes back, turn it up a little bit higher. The details of the scene become richer. He feels the sounds of the day he how warm it was. He could hear the birds chirping. The very rich experience could be reproduced. Somehow, we unlocked this memory.

He was in his 50s, and so this memory had been locked in his brain for the last 35 years. And with applying some electricity, we were able to unlock this memory from his brain. So we immediately thought, this is fantastic how one can stimulate in the brain and unlock an old memory. And this was indeed the idea that came immediately that perhaps this technique could be used to stimulate the memory circuits in the brain of patients to improve and enhance their memory. And this is where we got the idea of perhaps using DBS in exactly the same spot that we were trying to treat obesity, but instead using DBS to treat memory disorders to see if we could enhance memory. And the logical type of patient that we wanted to treat. Of course, are patients with Alzheimer’s disease, where there's a profound memory deficit. So on the basis of this serendipitous observation, we applied for and got permission to treat six patients with Alzheimer’s disease to see if one could safely introduce electrodes into their brain and stimulate their memory circuits to enhance and improve their memory and cognitive function.

BTB
And this became the first in human safety. Phase one trial testing the use of
Dr. Andres Lozano: that's right, yeah, this is this was only done in in our hospital. And in fact, that was more than 10 years ago now.

BTB
Yeah.

Dr. Andres Lozano
And since then, we moved from those six patients. We showed that it was safe. We showed that there was some patients that improved in their memory and that led to a phase two study in 40 patients. And currently we are performing an international study in 150 patients to see whether this is safe and effective and whether this could become a new therapy of deep brain stimulation to treat Alzheimer's disease.

BTB
Okay, so I want to drill down a bit into these results that you've been yielding over the last 10-11 years in terms of these trials, back to that first in human safety phase one trial. You proved it to be safe. Were you able to report in terms of patient benefit?

Dr. Andres Lozano
Well, what we were able to find is that in some patients, they improved or stabilized and other patients worsened. And what we found was that the patients had had very advanced Alzheimer's disease that were very impaired. They did not benefit at all. On the other hand, the patients who had mild symptoms that were forgetful, that couldn't remember things. They did get better. So on the basis of phase one, we narrowed down our patient selection criteria to those patients with moderate symptoms, mild or moderate symptoms, and we knew that it was not going to work in patients with advanced symptoms. So that is because the circuits in Alzheimer's disease deteriorate, they degenerate and in fact, they disappear. And once you have advanced Alzheimer's disease, when you can no longer remember your name or you don't recognize your children, these circuits are completely destroyed. And so we really cannot stimulate a circuit. There's nobody home to stimulate. And so from those observations, we narrowed it down to patients that were earlier on in their disease course where we could stimulate circuits that were still there and where there was a hope that we could drive the activity in those circuits and improve the patient's function.

BTB
So you go based on that safety phase one trial you mentioned you went onto the phase two trial with 42 people and you're now in the midst of a phase three, 150 person trial. What is your sense now, after 10-11 years of studying DBS, applying it to patients with mild Alzheimer's? What's your sense of how it's helping patients like, why is it helping patients?

Dr. Andres Lozano
What we know is that these circuits in the brain that control memory and cognitive function and Alzheimer's disease are underperforming. It's as if there's a dimmer switch and they are quite dim. And what we found is that by stimulating the circuits, one can

increase the activity. One can shine, you know, make the light brighter in these circuits, make the activity higher in those circuits. Whether that translates into a long term benefit is what we're trying to determine in a phase three study.

BTB
Right.

Dr. Andres Lozano
And in this particular study, it is a blinded study. So some patients get the stimulation and some do not. They all get the electrodes. And for one year, they are either turned on or not. And at the end of one year year, we see how the patients that had the electrodes turned on do compared to those patients that had the electrodes, but they were not turned on.

BTB
So that's a very rigorous trial. Actually, I, I want to ask you when you talk about electrical stimulation, what are we talking about here?

Dr. Andres Lozano
So what we're doing is delivering about three volts of electricity through the brain, and the patients are not able to feel this at all.

BTB
Wow.

Dr. Andres Lozano
Well, the patients are not able to tell whether it's on or off. And this allows us then to have a blinded trial where the patients are not able to guess neither the patients nor the doctors or anyone evaluating patients know whether the electrodes are on or off. And what this does, of course, is that it reduces the chance of a placebo response where if we do see a benefit, we can be quite sure that it is due to the electrical stimulation and not to some other placebo type response. I should emphasize that those patients that have the electrodes in but not turned on for a whole year after a year, we turn them on. So it is basically a delay of one year in one group versus the immediate turning on in the other group.

BTB
The region of the brain that you choose to stimulate for examining Alzheimer’s benefit, I understand that varies. Talk to us about the area or the region, the brain you choose to stimulate.

Dr. Andres Lozano
We are basically stimulating a circuit. So if you think of a circuit that goes from a to b to c to d and back to a, you have a choice of where to get on and where to get off on the circuit. So we've decided to stimulate at a particular area, which is at the confluence, a hub, if you like, within this circuit and where we are able to influence not only where we're stimulating, but all the downstream sites so very much like the spokes on a wheel, we're stimulating in the center. But then we're seeing the consequences of that stimulation spreading out along the spokes to activate many areas of the brain. And we find that particularly important because we know that there are many areas of the brain that are shut down or not functioning properly in Alzheimer’s disease. So we've chosen

an area of the brain that can influence not only what we're stimulating, but also the downstream targets from the brain.

BTB
and by sending these mild electrical impulses, are you simply overriding the degeneration of the brain due to the degrading effects of the disease? Or is the stimulation in some way restoring brain growth and function?

Dr. Andres Lozano
Well, you know, the brain is very much like a muscle. And you know, the more you use it, the more it grows, the healthier it's maintained. And so it looks like in Alzheimer's disease, these areas of the brain are underactive and they're atrophying. They're degenerating.

BTB
Right.

Dr. Andres Lozano
In fact, disappearing. And if we stimulate them, we now have some evidence that we can in fact restore the size and actually grow some of these areas in the brain back towards a more normal. So it looks like we are putting the brain in exercise mode where we're able to activate these areas of the brain. We're able to drive activity in these circuits and that appears to maintain the vigor and the integrity of those brain circuits.

BTB
And do you know why yet? Like, why there's growth of, say, the hippocampus associated with DBS treatment in Alzheimer's patients?

Dr. Andres Lozano
We know that when you stimulate a circuit in the brain, that there are trophic factors that are molecules that are released in that circuit. And in fact, we now know that there are growth factors that are released. And so our hypothesis is that in humans, when we stimulate these circuits, the brain's own intrinsic growth factors are being released, and these growth factors are then having an effect on growing certain areas of the brain, making more connections, even making more neurons.

BTB
And have you been able to measure the growth, Andres?

Dr. Andres Lozano
In humans we're able to measure the volume of the brain using MRI magnetic resonance imaging? So we're able to actually see that in some of the patients, the hippocampus grows in patients with Alzheimer's disease. And this took us completely by surprise as well, because the normal trend is for your hippocampus to shrivel up and disappear. So our expectation was that the patients would have their hippocampus shrink and disappear over time. But to our surprise, not only did it not shrink, but in some patients we saw the complete opposite. We saw that indeed, the hippocampus grew. And this is really unheard of that the hippocampus would grow in a patient with Alzheimer's disease.

BTB
There's another aspect of apparently my understanding from the research I did before talking to you today that there's another indicator of growth. Talk to us about glucose burn in the brain and how that could also perhaps be stimulating growth?
Dr. Andres Lozano
Yes, so the brain uses glucose as its fuel, and it turns out that in Alzheimer's, these are areas of the brain that are shut down, that are not burning glucose or not using. And it's as if the lights are out in certain areas of the brain. And we wanted to know whether the lights were out temporarily or whether we could turn them back on. Whether we could convince the brain to use glucose once again. And what we found even in our first six patients is that indeed we can restore glucose function in the brain. We can get brain areas that were previously shut down to light back up and to use glucose once again. And we find that particularly exciting because if we can convince the areas of the brain to use glucose again, it means that these areas of the brain are working once again. And if they're working once again, it means that the functions that have been lost as a consequence of the Alzheimer's disease may be able to return,

BTB:
And that could also stimulate or boost memory.

Dr. Andres Lozano
Absolutely. We think that there might be a reversible component where when you have Alzheimer's disease and you've lost some function, we might be able to turn the clock back and get those areas of the brain to go back online and to work once again.

BTB
And there's also electrical recording of a patient brain activity once they're on DBS. Talk to us about how this works and the purpose for doing that?

Dr. Andres Lozano
Well, what we know is that there are areas of the brain that are active and that their activity is a function of how healthy they are. And we're able to show that in Alzheimer's disease, the areas of the brain are somewhat quietening down. There's less electrical activity, again, the areas are to use the analogy with a dimmer switch. The activity is dim. And so we're able to measure the electrical activity using electroencephalography, using magnetoencephalography, these are various techniques, and we're able to show that by stimulating these areas of brain, we're able to re-establish the electrical signals, the electrical activity in these areas that were previously underperforming. So what we're basically able to do is to turn up the volume. We're able to turn up the dimmer switch to a more normal area because we can regulate the DBS because we can adjust just how much electricity to deliver. We can make sure that we stimulate just enough and not too much. So we're able to adjust and titrate just how much electricity to get the right amount of electrical activity re-established in the brain.

BTB
So 11 years on into your DBS trials with Alzheimer's patients, what are you able to report in terms of the staying power of DBS? Like, is this a lasting treatment potentially?

Dr. Andres Lozano
Well, we are in the midst of a clinical trial and the data is blinded, so we do not know, you know, we know how our patients are doing, but we do not know whether they're on

or off the stimulation because of the blinded nature of the trial. We will have an analysis in about one year, an interim analysis of how things are going and whether this looks promising, whether it looks safe. What I can tell you so far is that it is extremely safe that none of the patients in our studies there are now 45 patients in this current phase three out of 150, which is our goal. None of the patients have had any serious problems. No one's had a stroke. No one's died from the surgery. So it seems to be well-tolerated in patients with Alzheimer's disease.

What we have to determine now is how much benefit do these patients get? Are we able to put the brakes on in Alzheimer's? Because we know that this is an illness that progresses inexorably and we know that patients are going to deteriorate? So can we put the brakes on? Can we slow down their Alzheimer's? Can we improve their memory? And that is the questions that we're trying to address right now in use in doing this phase three study. If indeed, it proves to be a safe and effective therapy, then deep brain stimulation can become a new therapeutic option for patients with Alzheimer's disease. That would be extremely exciting because there are really no effective therapies for Alzheimer's disease right now.

BTB
So for the current trial, if there's perhaps listeners out there who are interested, what's the criteria for patient selection into this phase three trial?
Dr. Andres Lozano
Well, we are taking on patients who have mild Alzheimer's disease, who are on medication, who have tried medications and who are of any age. Our oldest patient is late 80s so far, but we can in fact even operate on patients that are in their 90s and they must be in the mild range. So this means people that perhaps are forgetful, people that perhaps cannot remember some details of names, people that may get lost if they were to travel in the city, but people who can dress themselves, who could take care of their personal hygiene, etc. So these are people that are mild but who have a clear impairment in their memory and who have tried medications. So these are really the criteria for enrolling patients. And so we would be very pleased to evaluate any patient that is interested in this, this trial.

BTB
The big picture. Where do you see the applications of DBS going?

Dr. Andres Lozano
Well, we know that we could stimulate any area of the brain, so I tell my colleagues that no area of the brain is safe from a neurosurgeon, we can really go anywhere now safely. And so we envisage that one could stimulate circuits that control your mood and perhaps treating depression circuits that control your appetite, controlling perhaps your weight, circuits that control your blood pressure, circuits that control your memory, etc. So really, anything that the brain does, we could adjust and think of it as a huge control panel with multiple switches, multiple circuits. Each one of these circuits does something different, and we can adjust the activity of each one of these circuits. So it's a question of choosing the right area of the brain, choosing the right patient. And of course, these are all experimental procedures that I'm telling you, although for Parkinson's, it is well established for the other indications that we're discussing. They are really at the cutting edge of the technology, and we're trying to push forward the frontier to see where indeed one can use DBS to treat these other disorders.

BTB
You're listening to behind the breakthrough the podcast, all about groundbreaking medical research and the people behind it at Toronto university health network, Canada's largest research and teaching hospital. I'm your host, Christian Coté. We're speaking with **Dr. Andres Lozano**, award winning senior scientist at UHN's Krembil research institute. Dr. Lozano's pioneering research in deep brain stimulation is made possible, in part thanks to generous donor support. If you'd like to contribute to dr. Lozano's groundbreaking medical research, please go to w ww.UHNfoundation. That's all one word. UHNfoundation.ca/podcast.

Andres, you were born in Seville, southern Spain and in the mid 60s when you were just two years old, your parents emigrated to Canada, settling in Ottawa. So as you're growing up, what's your recollection of that aha moment where you, you somehow knew you were drawn to the world of science and medicine?

Dr. Andres Lozano
Well, I knew that I wanted to be a neurosurgeon since I was a teenager and part of what, what that aha moment was actually watching television and watching Dr. Penfield, I mentioned him earlier. He was a pioneer neurosurgeon from McGill university, from the Montréal neurological institute, and indeed, dr. Penfield was operating on patients with epilepsy, and they too were awake and he was stimulating the surface of the brain. And he was able to produce also some very vivid memories when he was able to stimulate the brain. So sometimes patients felt like they could smell burnt toast, or they felt that they were in a certain scene. As a teenager, I found this is absolutely fascinating how one can use neurosurgery to unravel how the brain works, the mysteries of the brain. So I was hooked from that point on, and indeed I decided to become a neurosurgeon when I was a teenager and I actually went to McGill to train where dr. Penfield worked to learn those techniques. And then I eventually ended up in Toronto, where I was able to stand on the shoulders of this giant and to try to push that frontier even further.

BTB
But you've certainly done so. There's no question about that. I'm curious, though, this teenager, when you go to your parents to tell them, I want to be a neurosurgeon, what did they think of their son's newfound passion?

Dr. Andres Lozano
Well, yeah, they said, sure, you know, sure, honey, whatever you want, you know, whenever, whatever, I do this with my own children now, I mean, whatever they say, whenever they said as a teenager that they want to do certain things, you have to encourage them and you have to support them. So I was fortunate to have that encouragement and support from my family as well.

BTB
Talk to us then about mentorship along the way, how it shaped your career and how in turn, you approach mentorship?

Dr. Andres Lozano
Well, one of the greatest joys of my career has been to train neurosurgeons in these techniques and indeed we've been fortunate to train 70 fellows. So these are neurosurgeons that come from other countries to Toronto to learn these techniques, and they spend one to two years with us. They acquire this huge body of knowledge and

know-how, and then they go back to their own countries and then they become leaders in their own right in this way. So when I say their own countries, the majority of them have actually been Americans. So many of them have gone back to some of the most prestigious universities, like Harvard and university of Pennsylvania, et cetera. And then they've led initiatives in deep brain stimulation there. But we've also had doctors that have come from other countries all over the world and have been able to come, and they've enriched our lives and our scientific activity and have gone on to do great things for the patients in their own countries as well.

BTB
Is there sort of a practical type of advice that you offer them as they are on this journey with you?

Dr. Andres Lozano
I always tell them to be curious, to try to challenge dogma, to not accept anything as gospel, to be critical. I tell them that they should have at least one idea per day

BTB
Wow.

Dr. Andres Lozano
If they're, if they're not, if they don't have one idea per day, they're not, they're not thinking enough. And so we try to challenge our fellows, we try to push them. And really, when you do that, it's amazing how they rise above your expectations and come up with fantastic things.

BTB
We talked about your serendipitous moment in terms of your entree to applying DBS to Alzheimer's patients. I'm curious, has randomness or serendipity, does it have a role in scientific research or discovery?

Dr. Andres Lozano
It has a huge role, and probably the greatest discoveries have been serendipitous. And a good example is Alexander Fleming and the discovery of penicillin, where he noticed that there was an area of a petri dish that his bacteria weren't growing because of this mold had grown into his petri dish. And so that was the basis of discovering penicillin, which of course, has revolutionized modern medicine. So when you find something that you were not expecting, it is more likely to be real because you don't have a bias of selective attention. And so when you find something unexpected, it is probably for real and you have to pay a lot of attention instead of just dismissing a serendipitous finding. I think it's very important to pursue it and to find out what's the cause of it. Why is this occurring? Why are the bacteria not growing in this area of the dish? Why is this patient who I'm trying to treat their obesity, why is he telling me about his girlfriend when he was 20 years old? These, these are really the events that you could easily dismiss them and ignore them. But the real secret to advancing in science is to take those events seriously and to pursue them until you have a better understanding of what, what their cause is.

BTB
The flip side, I guess you could say, is challenges and obstacles and failure in your work in research, we're not really taught how to deal with failure in life. How do you navigate that in your research?

Dr. Andres Lozano
Failure is a normal part and an expected part of research, and many times you know you have to go down a blind alley to see to find out that it's actually blind. If you don't go down that alley, you'll never know. So we don't see failure as a negative, but rather as a means of focusing and of restating your scientific work and your, your hypothesis. So we see that failure is a necessary element to advancement in science. You have to fail and you have to rule out certain possibilities until you're left with inevitably the real answer that helps us tremendously because it helps us to focus and redirect our efforts. And it's very important to rule out certain things that are not right.

BTB
Now DBS surgery, you know, it involves this headgear where patients wear during the procedure that so that their head can be immobilized so they don't move, they're awake, they can hear the drills. It can all be a bit daunting or overwhelming. I'm curious to know what you think of the many patients who agree to be a part of your trials?

Dr. Andres Lozano
I think that you're quite right. It can be quite daunting and you have to really. I'm very impressed by these patients who are willing to undergo these, these procedures and who are active participants. I mean, they know that we need them. They know that they have to be awake and that they have to tell us what they feel. And so they are tremendously courageous to be able to, you know, allow us to do this and to really be full participants. So there's an element of they're doing it because they want to get better. But there's also and I've been very impressed by this, is this altruistic component where they feel that they're contributing to something bigger, that they know that what they are doing and what they're reporting will have consequences not only for them, but it may have consequences for many other people.

BTB
So there's sort of an altruism to their wanting to participate in your trials, and, you know, I had the privilege of interviewing one of your first DBS Alzheimer's patients 11 years ago. And I remember I still remember how, he said as a result of the procedure, he got his golden years back. What does that mean to you to hear that?

Dr. Andres Lozano
Well, it's extremely satisfying when you can take someone who has a very serious illness, a terrible illness where you know that their clock is ticking and it is only a matter of time until their memory is completely wiped out. And to be able to do something that might preserve their memory, preserve their ability to interact with their family, to talk to their children, to talk to their spouse, that is extremely satisfying. And so when we're dealing with these terrible illnesses like Alzheimer's that really wipe out your memory to do something. And this is why it's so important for us to continue our work is to take this challenge and to see what can we do to try to help these patients.

BTB
And you've been at this now about 30 years. What keeps you going?

Dr. Andres Lozano
For me, it is a couple of things, one is curiosity, the need to understand to better understand how the brain works, and every day I'm amazed by the things that we can

discover in the operating room. But the second thing is really to have impact and to have impact not only on our own patients, but to have international impact. If we discover a new treatment for Alzheimer's disease, this will have implications for millions of people and their families throughout the world. So that is what we're looking for. We're looking to influence not one or two, but millions of people, and we're fortunate to work in an environment where we can do this work and where the consequences of our work has the potential to improve the lives of millions of people.

BTB
As you move into the latter half of your career. Have you had the occasion yet to sort of reflect on your scientific research legacy?

Dr. Andres Lozano
So far, you know, we are so busy with doing the work and with, you know, trying to move forward on these various trials and various experiments that I haven't had too much time to think about that. But I do know that the legacy will be not only all the patients that we've been able to treat, but also all the people that we have been able to train throughout the world. And it is really through those people that the work that was done at our hospital in this field will continue for the years and decades to come.

BTB
You've maintained a very strong connection to your country of birth, and in 2007 you were awarded the order of Spain. I'm going to assume it was in large part because of your work, your pioneering work. That's one of the highest civilian honors in Spain. What, what did that mean to you?

Dr. Andres Lozano
Oh, that was a tremendous event, totally unexpected for me, but it really was a wonderful acknowledgement of our work and to be to be Spanish and to have Spain reach out and recognize our work was very, very humbling experience. I have strong ties to Spain, and one of my heroes is indeed a Spanish neuroscientist called Ramon y Cajal, who discovered that the brain was made out of neurons. Before that, people thought the brain was just a sponge jell-o. But he actually discovered that it was made of individual neurons cells. And so he won a Nobel Prize in 1906 for that. So there's a long tradition of fantastic work in neuroscience in Spain. And I was very proud to play a small part in that and to be recognized by that country.

BTB
Do you ever wonder what he would have said about your advancements in the field?

Dr. Andres Lozano
I think it would have been completely flabbergasted. He would have been so excited because he established that neurons spoke to each other, that one neuron spoke to another one and within a circuit, and to know that one could change the conversation of neurons by applying electricity and driving the conversation around neurons, he would have been pretty excited, I think.

BTB
So Andres, what's next for you? What should we be watching for over the next weeks, years to come?

Dr. Andres Lozano
we are using DBS in new indications as we described to, for example, control psychiatric illness to hopefully control things like your blood pressure, whether it's too high or too low. We might be able to regulate that by stimulating areas of the brain that control your blood pressure. We, of course, will continue with movement disorders. We are also looking at non-invasive ways of treating brain disorders. So without drilling a hole in your head using, for example, ultrasound to treat disorders of the brain to stimulate the brain through the skull. So we think that over the course of time, we will no longer use scalpels to do surgery, but rather surgery will be done non-invasively. And this will be very exciting because it means that we can treat more patients and will be, I think, very safe surgery. So we're going to see whether we can actually push the frontiers of this work towards doing surgery safer, doing surgery without having to open the head and to try to treat more and more patients.

BTB
Dr. Andres Lozano, award winning senior scientist at UHNs Krembil research institute, thank you for sharing your groundbreaking research with us and continued success.

Dr. Andres Lozano
Thank you very much Christian. It's been a real pleasure speaking with you today.

BTB
Dr. Lozano's research is made possible, in part thanks to generous donor support. If you'd like to contribute to his pioneering medical research, please go to www.uhfoundation.ca/podcast. And for more on our podcast, go to the website. Www. Behindthebreakthrough.ca and let us know what you think, we crave your feedback. That's a wrap for this edition of behind the breakthrough, the podcast all about groundbreaking medical research and the people behind it at the university health network in Toronto, Canada's largest research and teaching hospital. I'm your host, Christian Coté. Thanks for listening.