00:00:00:01 - 00:00:26:39
Leslie Schlachter
Hello and welcome back to the vitals, the Mount Sinai Health System's groundbreaking roundtable video podcast. I'm your host, Leslie Schlachter , a neurosurgery physician assistant here at the Mount Sinai Hospital. On this episode, we delve into the most sweeping and far reaching neuroscience studies in the history of medicine. The Living Brain Project, we're discussing all the major breakthroughs and what we know about brain science, and what these discoveries mean for you.

00:00:26:43 - 00:00:45:02
Leslie Schlachter
The patient to walk us through it. We're joined by Mount Sinai doctors, psychiatrist doctor Alex Charney and neurosurgeon Doctor Brian Kopell, who are experts in the field of neuroscience and are helping to lead this new project. Welcome, gentlemen.

00:00:45:07 - 00:00:54:41
Leslie Schlachter
So, as I said in your intro, you are a psychiatrist. You are a nurse, a neurosurgeon. I am. But what is the difference between neurology and psychiatry since there is so much crossover?

00:00:54:50 - 00:01:35:03
Dr. Brian Kopell
The way I look at it, I don't see a distinction between neurology and psychiatry. In fact, I think the distinction between the two is a vestige of sort of some anachronistic sort of thinking about the two entities at the end of the day. It's it's all, you know, it's all brain disorders. By the end of the day, and every sort of emergent behavior that comes from the brain, you know, is, is, you know, under the grand rubric of neurology and neuroscience.

00:01:35:07 - 00:01:50:52
Dr. Brian Kopell
Right. I mean, I mean, in essence, you are a a limbic neurologist, right? You know, in that regards. Right. Your your neurology happens to focus on what we, you know, colloquially call the emotional circuitry or the limbic circuitry of the brain.

00:01:51:05 - 00:02:19:13
Dr. Alex Charney
Yeah. I think the distinctions are, you know, artificial. They're they have historical explanations as to why psychiatry, neurology exist as two separate clinical disciplines. You know, on the science side, there isn't that distinction. So people who train as like PhDs in neuroscience, for example, don't specialize in, disorders of that are classically considered psychiatric versus neurological.

00:02:19:13 - 00:02:41:33
Dr. Alex Charney
So that when I did my training in the genetics of brain disorders, it wasn't like the the methods you use to understand the genetics of the brain differ for schizophrenia versus like, like multiple sclerosis. It's

the same principles. So on the science side, there isn't this distinction. It's all in the brain. Or.

00:02:41:33 - 00:02:58:19
Leslie Schlachter
Like in a book. Right. Because like psychiatric diagnosis is are like literally in a book. Right. The DSM. Right. And there's not like generally neurologists there is crossover in how they treat them. But like there's a book for psychiatric illnesses versus neurologic if we want to make it black and white.

00:02:58:24 - 00:03:20:24
Dr. Alex Charney
There is although the origins for that system are, you know, I think sometimes psychiatry gets this rap of like, we have this very subjective diagnostic system because there is this book. But in reality, other medical specialties are, just as subjective. And the criteria for diagnosis, they just don't formalize it in a book. And the way psychiatry.

00:03:20:29 - 00:03:30:03
Dr. Brian Kopell
Is very much is about the neurological exam, which is inherently subjective right, by definition. And so there is that sort of kind of similar analogy.

00:03:30:03 - 00:03:31:50
Dr. Alex Charney
Right. Absolutely.

00:03:31:55 - 00:03:48:27
Leslie Schlachter
So I mean, I feel bad asking like, what do we know now about neurology in neuroscience now that we didn't know 20 years ago? Like what are the biggest game changers? But like, let's just like psychiatry, we have to throw that in there. Sure. So what would you say are kind of like the most shocking things that we know now that we did in 20 years ago.

00:03:48:27 - 00:03:50:48
Leslie Schlachter
And like, how did we learn to know that?

00:03:50:52 - 00:04:24:18
Dr. Alex Charney
Yeah, I could I could take that one from, you know, where in my heart, as a, someone who focuses on the biological underpinnings of these conditions, like neurological and psychiatric conditions, the main thing we've learned over the last 20 years is about how, the genetics of these conditions that passes from one generation to the next. If you're looking at the field 20, 30 years ago, there was this, well, what you could think of as, like, single gene, single disorder mindset of this particular gene is why you are this way.

00:04:24:23 - 00:04:45:24

Dr. Alex Charney
You just colloquially still talk like that, like, oh, I have the gene for being crazy, you know, in my family or something like that. What we know now is that, the genetic architecture we call it, of these conditions is, is highly complex. There is no single gene for, say, a condition like schizophrenia or depression or a Parkinson's disease or Alzheimer's disease.

00:04:45:28 - 00:05:05:15
Dr. Alex Charney
There are in individual families there could be a single gene. That is the main cause. But across the whole population, these conditions are highly what we call polygenic. There's there's areas throughout your genome that are each contributing to your risk. A little bit. Collectively, they all add up to, to increase your risk. A lot, but in ways that we don't still don't quite understand.

00:05:05:15 - 00:05:17:24
Dr. Alex Charney
But but that basic notion of poly genus and the complexity of these heritable conditions is, is, in my opinion, the main thing we've learned over the last 20 years with respect to like their root cause.

00:05:17:29 - 00:05:25:12
Leslie Schlachter
Like what disease states would you say has that knowledge affected the most if regarding like diagnosis and treatment?

00:05:25:17 - 00:05:51:13
Dr. Alex Charney
The knowledge hasn't really had clinical translation yet. So, you know, I would say, conditions on the psychiatric side, there is no condition that really does not fall into that category of, of our understanding of its root cause at the genetic level. Hasn't changed over the last 20 years. That's not really true for any psychiatric disease, because genetics has, has, has changed our understanding more or less of all of them.

00:05:51:18 - 00:06:02:01
Dr. Alex Charney
But it hasn't changed how we treat them. So that that translational gap is, is critical. And you probably make the same argument for disorders across neurology.

00:06:02:06 - 00:06:25:10
Dr. Brian Kopell
You know, building on that, you know, in a general sense, what what has happened in the last 20 years in neuroscience, etc., sort of parallels, you know, other aspects of our life is just this explosion of data, right? You know, 20 plus years ago, it was a heroic effort to sequence certain genes. Now, you know, we are able to do that at scale.

00:06:25:12 - 00:06:58:44
Dr. Brian Kopell

That's a massive amount of increased information. You know, same thing with with imaging of the brain, right. You know, we used to be only be able to sort of image the brain from an aspect of gray versus white matter. Right? The self versus the white matter of the brain. And now with, you know, track to graphic analysis with resting state connectivity, we can have a like an entirely new sort of, dimension of how we can sort of look at the brain.

00:06:58:44 - 00:07:09:07
Dr. Brian Kopell
Right. And so what the sum total of all this is, is, I think what we're beginning to see is a challenge of this sort of.

00:07:09:12 - 00:07:09:54
Dr. Alex Charney

00:07:09:59 - 00:07:23:04
Dr. Brian Kopell
19th and 20th century sort of definition of disease. Right? We think of like Parkinson's disease or OCD or depression as we learn in medical schools. These are separate.

00:07:23:04 - 00:07:23:51
Leslie Schlachter
Diseases.

00:07:23:57 - 00:07:51:31
Dr. Brian Kopell
Right, right, right. With giant walls around them. And and, you know, never shall the pass between the two. But as we are able to look at more and more of this data, what we're beginning to see is something like Parkinson's and something like depression has this incredible overlap, of their basic underpinnings, and that these separate diseases are, in fact, not.

00:07:51:32 - 00:08:03:18
Dr. Brian Kopell
It's like a continuum. And and the idea of being able to look at these entities as a continuum, I think, is a really game changing way that we're going to develop therapies in the future.

00:08:03:23 - 00:08:21:34
Leslie Schlachter
So we're here today because we're talking about the Living Brain Project. And I learned about this a couple of years ago. I work I'm the physician assistant who works with Doctor Joshua better said. And I thought Living Brain project. What does that mean? It means you're actually taking pieces of people's brain to learn from them. Can you like, what does this project look like?

00:08:21:34 - 00:08:23:39
Leslie Schlachter
How did this come to be and what are your goals?

00:08:23:43 - 00:08:24:51
Dr. Brian Kopell
You want to take that one or.

00:08:24:54 - 00:08:26:35
Leslie Schlachter
That's a big one.

00:08:26:40 - 00:09:00:54
Dr. Alex Charney
I could I'll take it from my perspective, right? I probably have the right interesting but related, perspectives of how it started. Yeah, for me, it started, when I was a trainee, who was coming into this field of studying the biology of brain conditions, but specifically schizophrenia. That's been my my focus throughout my career. And, you know, learning that the main way we were studying how our brain works at the biological level, and this is probably like ten, 12 years ago, something like that, was through studies of, brain tissue from people who've passed away.

00:09:00:57 - 00:09:23:09
Dr. Alex Charney
Right. Which, you just as a clinician felt like to me intuitively off, like, how am I supposed to understand the basis of people who are hallucinating, hearing voices that aren't there, or or having delusions? You know, these false fixed beliefs? How am I supposed to study the biological mechanisms of that? And someone whose brain is no longer functioning, right.

00:09:23:18 - 00:09:41:04
Dr. Alex Charney
Was passed away. So it just got me thinking of, like, how why don't we study the biology of the brain? In people who are alive and, was just kind of met with, skepticism from my colleagues in the field, like.

00:09:41:11 - 00:09:43:36
Leslie Schlachter
Like who's going to sign up to have a piece of their brain removed?

00:09:43:40 - 00:10:15:52
Dr. Brian Kopell
Or how about the the almost silly notion that there was controversy about the idea that there's a difference between a living brain and a dead brain? I mean, yeah, that's it. I mean, the only in academics can you have a knock down, drag out fight about something that a seven year old would be like, look at you. Like, of course there's a difference between a living in a dead brain and, you know, I, I like diving head forward into these kind of controversies.

00:10:15:52 - 00:10:19:14
Dr. Brian Kopell
Right. Because that's where the interesting stuff is.

00:10:19:19 - 00:10:44:13

Dr. Alex Charney
Right? Absolutely. And the another thing that people said at that time and still so today, is that, well, if your interest is in disease X, say depression, schizophrenia, whatever it is. Well, the people who get neurosurgery, which are the only people you can whose brain you can theoretically even consider studying when they're alive. Well, they they're getting their surgery because something's wrong.

00:10:44:18 - 00:11:18:18
Dr. Alex Charney
So you can't learn something about how the brain works normally or how the brain goes awry in your condition of interest. If you're studying people who are getting brain surgery for some other reason. Right. And I think that's a fundamentally flawed notion. And also, when you think about what they're what they're with, they're missing when they say that, because they're implying when you study someone who's passed away because you could get the brain of someone who had the depression, schizophrenia, when they're alive, you can you can theoretically get brain tissue from those people when they pass away.

00:11:18:18 - 00:11:32:06
Dr. Alex Charney
So therefore you can study those diseases. It's ignoring the fact that they have they have the worst brain problem, right? The brain problem where nothing works, your brain goes completely awry, which is death. Right? And that's something that is is ignored in the field.

00:11:32:11 - 00:11:46:58
Leslie Schlachter
You access the brain regularly, right? Can you just tell our audience? Because what you do is so incredible. I've seen it with my own eyes, and I've watched you listen, can you just explain what you do and why you do it? So that we know how you guys came together, right?

00:11:46:58 - 00:12:13:19
Dr. Brian Kopell
So, my my sort of, one of the main things that I do in my neurosurgical career is a type of procedure called deep brain stimulation, which, in sort of most colloquial terms, is a pacemaker for the brain. And, in this sort of pacemaker analogy, we have an electrode that goes into the brain, into a specific circuit of the brain.

00:12:13:24 - 00:12:32:45
Dr. Brian Kopell
And then it's attached to a pacemaker unit that drives electricity into the brain and modulates the electrical activity. And we, as a result, help people. So part and parcel of of this, of this approach is you have to gain access to the brain, which involves, drilling a hole in the skull.

00:12:32:45 - 00:12:37:09
Leslie Schlachter
Well, first you need to get the patient in your door and get them to agree to like you. That's of course, that's not right.

00:12:37:10 - 00:13:21:42
Dr. Brian Kopell
That's a that's a separate thing. But like, let's assume all that has occurred. And so how do you put an electrode into the brain. Well, you have to drill a hole. Right. And so the hole gives you a certain access to a piece of exposed brain. And the reason why we, approach the brain in a particular way is because we know, after decades and decades of intervening with the brain, that there are avenues of access to the brain that are, in the sort of neurosurgical sense, safe, meaning you can traverse them with essentially very little impact in a patient's, you know, neurological functioning.

00:13:21:46 - 00:13:23:02
Leslie Schlachter
Eloquent versus not eloquent.

00:13:23:02 - 00:13:41:33
Dr. Brian Kopell
Right? Yeah. That's the sort of sort of the old school way of talking about it. And, you know, of course people can like dance on a pin and basically say, well, what is eloquent, what is not eloquent? My whole brain is eloquent, blah, blah, blah, blah. Okay. But there are there are avenues safe traversing avenues that you can access the brain.

00:13:41:42 - 00:14:04:58
Dr. Brian Kopell
And we do that with deep brain stimulation. So the implication is, is, you know, when before we put the electrode in, you have to prepare the surface of this little brain area so that the electrode goes in with as little bleeding as possible. And, you know, the brain is covered by a covering called the pia arachnoid, which can be tough in other in certain people, and it can deflect the electrode.

00:14:04:58 - 00:14:24:50
Dr. Brian Kopell
So you want to make sure that is taken care of because again, you know, like, you know, deep brain stimulation is like real estate. It's all about location, location, location, location. Right. And so if you're off target, you don't get the results you want. So the idea being is that in order to prepare the surface, you know, I typically and others do as well.

00:14:24:50 - 00:14:39:27
Dr. Brian Kopell
It's pretty common in the in the neurosurgical approach is you take electric tweezers and you kind of cauterize a little tiny portion of the brain. Well, when you cauterize it, you cook the brain. And so you render that part of the brain essentially inert.

00:14:39:37 - 00:14:41:01
Leslie Schlachter
Right, right, right.

00:14:41:06 - 00:15:06:56
Dr. Brian Kopell
This gives us an opportunity in certain patients, if they agree to do so, to take a little grain of rice piece of that brain prior to placing the electrode and prior to coagulating the brain. And so this gives us this really unique opportunity to gain a sample of living brain, that would essentially have, no impact on a patient's otherwise well-being.

00:15:07:01 - 00:15:12:45
Dr. Brian Kopell
But can potentially move the needle seriously or move the ball down the field in neuroscience.

00:15:12:52 - 00:15:33:24
Leslie Schlachter
All right. So for what I do and people who have watched before know I'm a neurosurgeon. EPA it sounds so crazy to me. You're talking about like a grain of rice level. But for us, we will literally take a whole hunk of the frontal lobe to remove a meningioma or like a big chunk of cerebellum, right? If we have a, you know, huge posterior fossa surgery.

00:15:33:28 - 00:15:40:04
Leslie Schlachter
Are we talking, like just cerebrum is helpful to you, or cerebellum also helpful to you? Because I feel like we could be sending you guys hundreds.

00:15:40:08 - 00:15:40:39
Dr. Alex Charney
So at.

00:15:40:42 - 00:15:41:26
Dr. Brian Kopell
This point.

00:15:41:31 - 00:16:03:47
Dr. Alex Charney
This is this is a this is a really important point. And this is how I think the Living Brain Project model, scales and becomes, you know, a paradigm shift in the field because, sampling the prefrontal cortex of DBS patients is an incredible achievement as, just a really practical insight that Brian had all those years ago.

00:16:03:52 - 00:16:11:09
Dr. Alex Charney
That's now we have collected over I think, approaching a thousand biopsies aren't the exact number. But, you know, by far the largest.

00:16:11:11 - 00:16:12:36
Leslie Schlachter
At your website, it says 300.

00:16:12:39 - 00:16:46:43
Dr. Alex Charney

Yes. Where were that? And so it's it's it's definitely like the largest collection of, like, human brain tissue for research from living people that I know of, you know, and, but how do you, how do you scale this and make the general principle of leveraging access to the brain in the neurosurgical operating room as a, a way to advance neuroscience, and that's, through doing what you're describing, which is taking a survey of the whole neurosurgical field and saying, where are opportunities for tissue collection and banking that happen all the time that we're just not taking advantage of?

00:16:46:48 - 00:17:03:10
Leslie Schlachter
Yeah. I mean, I can imagine, like there's cases that we do like big skull based tumors where I know I can I mean, I can think of hundreds of patients over the years that we've been like, sure, take it. But then there's like GBM patients where like it's, you know, they're they're fighting for like every little piece of their brain to be spared.

00:17:03:10 - 00:17:16:39
Leslie Schlachter
But all right, we're getting off topic. So you guys, you are like, what's happening at the brain level? Because before Living Brain, you're basically talking to patients, examining them, getting scans, labs, genes. Now you actually have tissue.

00:17:16:44 - 00:17:44:38
Dr. Brian Kopell
And more and even more importantly. So you just described different lenses into brain function, into living brain function. But typically in order to sort of do that, you had different studies, like one imaging study on a lot of individual brains, or you had, you know, a lot of genetic studies on a lot of dead brains or a lot of studies on EEG.

00:17:44:42 - 00:18:12:09
Dr. Brian Kopell
Right. What's really cool about the Living Brain Project? What really resonated with me is that all of these different lenses are converging on a single individual brain, so we're not having to make this sort of inherent meta analysis of synthesizing individuals from 10,000 people of different data sets and kind of creating this sort of meta sort of model of how the brain functions.

00:18:12:09 - 00:18:17:25
Dr. Brian Kopell
We now are able to take all of these lenses in a single human brain.

00:18:17:31 - 00:18:21:31
Leslie Schlachter
So what's the question you're asking? Like, how did you get this approved?

00:18:21:35 - 00:18:44:49
Dr. Alex Charney

Okay. So we got approved by. Yeah. The concept is, is that, what's the risk for the patient? Yeah, that's that's all. That's all any regulatory agency cares about. And in this case, because the patient is losing the tissue through the colonization process, the risk. Yeah. Is is not the right. People pick apart the word to use and how you describe the risk.

00:18:44:49 - 00:19:02:16
Dr. Alex Charney
It's, it's it's not that it's non-trivial, but intuitively, the patient's going to lose more or less the same amount of tissue in the two options, with or without the biopsy. So the risk should be pretty minimal. So that's, that's essentially how you get approved for the overall, collection of the tissue. And then what's the question you ask?

00:19:02:16 - 00:19:22:16
Dr. Alex Charney
Well, with this framework in place, there's, there isn't. It's one of those things where it's it's not a single question study. It's more of like a, like a, like a framework for studying the brain. And then under that framework you could ask many questions. I'll give you an example of, of, of a really intuitive thing that this design allows you to do that we couldn't do before.

00:19:22:21 - 00:19:38:25
Dr. Alex Charney
You think of, like taking your blood and like measuring something in your blood that would tell you, like, what's going on in your brain, like we call these things biomarkers, like the general notion that you could use a blood sample to, like, diagnose something going on in the brain or predict something is going to happen in the brain.

00:19:38:25 - 00:19:58:28
Dr. Alex Charney
And this this is something that's all over the place. You always, you see, like, you know, some new test for Alzheimer's is out there. It's like it's measuring something in the blood. That's, that's, that's that's saying what's going on in the brain. The if you think about, well, how what would you need to do in order to know how you can use a blood sample to say what's going on in someone's brain?

00:19:58:28 - 00:20:14:26
Dr. Alex Charney
Well, just what would be the right study design to even create that knowledge base? Well, you would want to have blood from someone and their brain at the same time, right? And you want to do that in a lot of people, and you want to profile the blood and profile brain and look at how is what you see in the blood related to what you see in the brain.

00:20:14:31 - 00:20:25:21
Dr. Alex Charney
Well, that study has never been done that. So like everything we know about trying to like, measure, use the blood to like, measure, what's going on in the brain is it's not based on the correct study design.

00:20:25:33 - 00:20:29:12
Leslie Schlachter
So what do you even know what we are going to know? Well, you guys might know now.

00:20:29:16 - 00:20:29:27
Dr. Alex Charney
We're.

00:20:29:36 - 00:20:31:30
Dr. Brian Kopell
Just beginning. We're just beginning. I mean.

00:20:31:35 - 00:20:33:15
Leslie Schlachter
What have you learned so far?

00:20:33:19 - 00:20:42:58
Dr. Alex Charney
So I'd say the key things we've learned from the Living Brain Project, number one is that, you can collect brain tissue from living people in a safe way. That's a that's a key.

00:20:43:03 - 00:21:06:51
Dr. Brian Kopell
You know, we we just published that in, like, over 12, 12 or 1300 implementations. And we looked at between, you know, there were roughly half and half, and we looked at all of the safety data that we typically look at. And a deep brain stimulation operation, anything from cognition to bleeding to seizure to infection. And there just is no difference whether I took a biopsy or not.

00:21:06:55 - 00:21:12:41
Leslie Schlachter
So you're looking like obviously retrospectively to patients that you did in versus the patients that you asked about the same. Yes.

00:21:12:41 - 00:21:19:46
Dr. Brian Kopell
Okay. Yes. And so as as Alex points out, we can do this safely at scale that, you know.

00:21:19:51 - 00:21:21:57
Dr. Alex Charney
That's when they when we first proposed the study.

00:21:21:57 - 00:21:22:28
Leslie Schlachter
Biggest thing.

00:21:22:30 - 00:21:26:07
Dr. Alex Charney
The first thing people said that you can't do that. Well, you can't do it. It's safe.

00:21:26:18 - 00:21:30:57
Leslie Schlachter
I remember I remember hearing those conversations and I was like, guys, we're talking about the smallest little bit.

00:21:31:03 - 00:21:31:22
Dr. Brian Kopell
Yeah.

00:21:31:25 - 00:21:32:07
Leslie Schlachter
Is anyway.

00:21:32:07 - 00:21:33:46
Dr. Alex Charney
Right. People said that weren't neurosurgeons.

00:21:33:46 - 00:21:55:18
Dr. Brian Kopell
Yes. Or or it depends on the type of neurosurgeon. But like most, most bread and butter neurosurgeons, if you were to ask them, what do you think the effect is of taking a tiny piece of, of of of prefrontal lobe of the brain in terms of someone's function. They would just they would probably like laugh. They would laugh at first just in a way that it only a neurosurgeon.

00:21:55:28 - 00:21:57:16
Dr. Brian Kopell
What to that kind of question.

00:21:57:21 - 00:21:59:31
Leslie Schlachter
You'd have to be in a neurosurgical O.R. to be like.

00:21:59:43 - 00:22:00:55
Dr. Brian Kopell
Of course, if.

00:22:00:55 - 00:22:01:18
Leslie Schlachter
You get it.

00:22:01:22 - 00:22:10:14
Dr. Brian Kopell
Right. And so, you know, but of course, there's always, you know, yeah, opportunity for controversy, you know, in anything that we do, basically.

00:22:10:19 - 00:22:15:34
Dr. Alex Charney
The second thing we've learned is that that living and postmortem brains are not the same at the molecular level, which.

00:22:15:34 - 00:22:17:06

Leslie Schlachter
See. Yes. Okay.

00:22:17:11 - 00:22:19:44
Dr. Brian Kopell
Your seven year old was correct. Basically there is.

00:22:19:55 - 00:22:21:43
Leslie Schlachter
Like what's the biggest thing that you've learned so far?

00:22:21:57 - 00:22:45:40
Dr. Alex Charney
If you measure the types of things we measure in these brain samples are, gene expression levels, transcriptome wide studies. We measure the expression level of every gene. You can detect every protein. So you're talking testing tens of thousands of genes, tens of thousands of proteins. So, more or less, it seems like there's statistically significant differences between the living and postmortem state with respect to, like, every gene and every protein.

00:22:45:45 - 00:22:57:01
Leslie Schlachter
What are you doing with this piece of tissue? Like, is it just like one tissue going one piece going on one slide multiple? Like, how are you fixing it? And how are you? Because you want to have a database to look for it in the future.

00:22:57:01 - 00:23:21:40
Dr. Alex Charney
So how you the general principle when you take a biopsy is is to keep it in as pristine condition as possible, to leave open the opportunity to do as many things down the road with it as possible. Right. Depending on what you want to do with it, you may have to process this specific way at the point of collection, which then oftentimes requires like you've essentially committed to a specific path of like only doing that particular test on that sample.

00:23:21:45 - 00:23:43:34
Dr. Alex Charney
So we try and, process the sample away at the point of collection. That leaves open the most possible things we can do with it down the road. So, for a given biopsy from surgery to surgery, we may not be using that tissue for the same exact set of things. So, for instance, one interesting thing that we published recently in, this journal, Nature Biotechnology, this is work led by our colleague Joe Dong.

00:23:43:39 - 00:24:12:01
Dr. Alex Charney
He, he reached out to us learning about this. The brain project asks us if we could, spare, 3 or 4 biopsies, because he had developed a mechanism to deliver, gene therapies to the brain in mice. And he wanted to verify that when, treating human brain tissue with that, it's essentially like a

new kind of pharmacology, that he can show that this, that this, delivery system delivers genes to the human brain.

00:24:12:14 - 00:24:19:04
Dr. Alex Charney
Wow. So he, you need living human brain tissue to do this, right? Because it's like you're essentially treating how long you.

00:24:19:09 - 00:24:21:05
Leslie Schlachter
Stay alive for.

00:24:21:14 - 00:24:36:32
Dr. Alex Charney
Yeah. It's a good question, and I don't. The answer is it depends on how you process it. If you get it right from the O.R. to the lab, you can keep, the brain, that tissue functional for assays like this, for, you know, an hour or two. But we haven't systematically.

00:24:36:32 - 00:24:39:18
Leslie Schlachter
Made that sound like that was a long time. Like that's not very long.

00:24:39:19 - 00:24:44:39
Dr. Alex Charney
No, it's not very long. Yeah, but it's just long enough to do something. And you probably keep it a lot longer if you came up with like, creative ways.

00:24:44:40 - 00:24:49:28
Dr. Brian Kopell
Right, right. So there's an opportunity to keep it, you know, to learn how to figure out how to keep it alive longer.

00:24:49:28 - 00:24:59:12
Leslie Schlachter
Yeah. So for people listening, this is like a really big deal. Like you guys have moved the needle in research that like, is anybody else doing anything like this?

00:24:59:16 - 00:25:22:01
Dr. Alex Charney
There are other groups that, have studied, but. Well, I'd say if you back up what we're doing is not, is not actually that novel like as if it's almost like rediscovering an approach that's, like as old as, as neurosurgery and psychiatry, neurology itself, like, you think of, like, Wilder Penfield and like the human homunculus that we all have to learn.

00:25:22:06 - 00:25:44:27
Dr. Alex Charney
Right. Like, it's like this notion of how the brain is organized, and what areas of the brain do what these came from innovative studies performed in the operating room, like bringing together neurosurgery and neuroscience. So I actually think what we're doing is essentially like,

the same philosophy is just like, updated for, like, using, like state of the art technologies, like genome sequencing and whatnot.

00:25:44:36 - 00:25:53:49
Leslie Schlachter
I guess it's like what you were talking about, the beginning is like all of this information that we've that you've gotten over the last 20 years, you can actually now use it that you have you're getting a living brain. Right? Okay.

00:25:53:51 - 00:26:23:24
Dr. Brian Kopell
And I and I and the tools that we have to sort of deal with these growing high dimension data sets is getting better. Like, we're better. We're we have more tools today to deal with more information than our colleagues from decades ago. Right. We have computers. We have now machine learning tools and things of that nature that we can now begin to take these incredible data sets and do something even more interesting from it.

00:26:23:29 - 00:26:49:03
Dr. Brian Kopell
So the, you know, novelty, novelty very often comes from revisiting the old and doing it in a certain and, and sort of in a new way, basically. Right. Because, you know, like you look in the Bible and, you know, King Solomon said there is no new thing under the sun. So there's this notion that goes back to antiquity, that novelty is a very funny, cyclical thing.

00:26:49:03 - 00:26:58:17
Dr. Brian Kopell
Right, right. And I think the same thing is here as well, where we are, we're doing something that is very old in a very new way.

00:26:58:17 - 00:27:20:06
Dr. Alex Charney
Yeah. It's a it's like the it's the whole notion that the people who were who I was being exposed to when I started the Human Brain Project with Brian, the people who are doing the work on the genomic side and, you're trying to understand the biology of, of, of these conditions that that they were not working at all with neurosurgeons.

00:27:20:06 - 00:27:51:46
Dr. Alex Charney
I mean, when you think about that, that's that's crazy. How could yeah, how could the world's leaders in studying the biology of the human brain not be working hand in hand with the people who hold the human brain in their hands and look at people, and, and and no one was doing it. And so that it just seemed like if you really want to understand how our brains work, neurosurgeons and, the, the, the people studying the biology of the human brain need to be working, like, hand in hand.

00:27:51:46 - 00:27:52:45
Dr. Alex Charney
Right. And they were.

00:27:52:54 - 00:28:17:55
Dr. Brian Kopell
Right. Like. And that goes back to the original question you asked, like, how did this all come together? And for me, you know, just personally, the thing that resonated with me growing up as a kid was, you know, the Apollo program. And what was the essence of the Apollo program? It was the coming together of different disciplines to pull in a certain direction to make a miracle happen.

00:28:18:00 - 00:28:18:25
Dr. Brian Kopell
We landed.

00:28:18:28 - 00:28:31:12
Leslie Schlachter
So what's so what's our miracle here? Like like, I know you guys, you're gathering all this information, but for, like, patients listening in for me who, like, I understand everything you're saying. I want to know. How is that going to help me? Yeah, for my job.

00:28:31:13 - 00:28:49:46
Dr. Alex Charney
So when I think of it the way I explain to people as you think about, know the course of your day, all the things you feel and experience, you know, it's like you feel, you feel sad or you feel happy or you drink some coffee and you got a pep in your step, or, you know, you feel bored listening to a podcast, someone talking about the brain.

00:28:49:51 - 00:29:12:46
Dr. Alex Charney
Like over the course of your day, your brain is doing all these incredible things and and all of that ties into to to mental illness and, and neurological illness, all of those, those those brain functions. And if you ask, well, what's what's happening inside my brain, like, as I'm experiencing those things, like when my mood goes down all of a sudden because I just learned that, you know, something bad happened, like, so like I lost a loved one.

00:29:12:46 - 00:29:34:55
Dr. Alex Charney
Like what happened inside my brain. This is the study that needs to be done to answer those questions. At the most basic level, it hasn't been done before. We have the technology to do it now. So that's the moonshot is really being able to make this map between, how our brain is functioning at the most, the deepest biological level and then our subjective experience as human beings.

00:29:35:00 - 00:29:36:55
Dr. Alex Charney
Making that connection is what the human brain projects.

00:29:36:55 - 00:29:47:35
Leslie Schlachter

Although if you were to guess a timeline on when there would be, like, not earth shattering, but just like, wow, helpful information. When do you think that would be?

00:29:47:40 - 00:29:58:37
Dr. Brian Kopell
Well, I would argue that Alex has already given an example of it, the development of a new tool to to to treat patients with Alzheimer's. Right. So I'm just saying we're really just scratching the surface.

00:29:58:42 - 00:30:02:21
Leslie Schlachter
To be clear. You mean the development of tool like so that blood test.

00:30:02:25 - 00:30:30:39
Dr. Alex Charney
So I think I think the the most right to say the most practical thing for patients, okay, that the human brain project has led to today would be that we have used the tissue that we collect in this way to show that new a new class of drugs, which can be thought of as like the next generation of medicine, that, that they work, they get into the brain tissue of people.

00:30:30:52 - 00:30:31:42
Dr. Alex Charney
And now the drugs.

00:30:31:42 - 00:30:32:11
Leslie Schlachter
Are we talking.

00:30:32:11 - 00:31:02:06
Dr. Alex Charney
About? They're they're they're they're called gene therapies. Okay. So these are drugs that you can, deliver through, intravenous injection. Okay. And they allow you that the drugs go into the brain and you can now modulate essentially any gene. Okay? Right. In the past, you think of pharmacology, you've got a couple hundred genes that you could target through, through all of the drugs that exist in the world that are like, approved for use in humans right now, this technology opens up, the druggable genome, what we call it, it's averaging in our body.

00:31:02:06 - 00:31:03:13
Dr. Brian Kopell
So kind of let me.

00:31:03:14 - 00:31:04:46
Leslie Schlachter
Give you there's like, so many things.

00:31:04:46 - 00:31:05:16
Dr. Brian Kopell
Yeah, there.

00:31:05:16 - 00:31:07:03
Leslie Schlachter
Is something it's so painful.

00:31:07:03 - 00:31:27:00
Dr. Brian Kopell
So another study that we recently published and it's one of the my, my sort of sort of one of my favorite things was the, you know, when we asked ourself the question, so during the course of a deep brain stimulation procedure, I record neural activity deep in the brain near the target.

00:31:27:01 - 00:31:28:52
Leslie Schlachter
These are the ways.

00:31:28:57 - 00:32:13:55
Dr. Brian Kopell
They can be better ways. But we're actually recording single single neuron recordings. So beta waves are the confluence of many neurons working together. One of the actual signals that we record during deep brain stimulation is single unit recording. So just a single neuron, we get a lot of electrophysiological signals from multiple single neurons. And so we sort of just ask the question, is there something that we can correlate and we can connect of the expression of the genes at the surface with these neurons that are, you know, for all intents and purposes, a universe away, because, again, you know, the distances in the brain, the brain is all interconnected.

00:32:13:55 - 00:32:42:11
Dr. Brian Kopell
So even though the distance is large, things work together. And the idea that there may be some genetic sort of link between that and the activity was sort of like, well, maybe, but it's it's hard, you know, there's there's not a direct connection. So it was like, well, you know, it seemed like a long shot if. Well, and lo and behold, what we found is in fact, there is a connection.

00:32:42:16 - 00:33:04:46
Dr. Brian Kopell
And so why is that interesting? Well, it's interesting if you're, if you're a neuroscientist just from the, the notion of it. But here's something that, you know, you want to talk to your, your lay your lay audience like, how is this going to affect me? Well, as a neurosurgeon that's interested in putting devices in the brain, people now have all heard about brain computer interfaces, right?

00:33:04:51 - 00:33:30:41
Dr. Brian Kopell
And so right now, these devices are relatively dumb. They're just electrodes that are placed on the brain. And then we have to deal with the information. But you can imagine the data that we are collecting in this type of process could create a data set to teach a brain machine

interface to work really well. Maybe you want you know, right now we conceive of brain machine interfaces as just affecting motor function.

00:33:30:41 - 00:33:49:21
Dr. Brian Kopell
Moving right. But in principle, this kind of data with electricity, we could potentially influence gene expression if done in a sort of granular way. I mean, again, I am talking in a sort of loose way, but that's the that's what the potential is for this type of.

00:33:49:21 - 00:34:17:16
Leslie Schlachter
I mean, I'm thinking about like I've done so many podcasts now on issues that like I'll just autism, for example, like when I, I'm, I feel bad, I'm blanking on his name. But, he was saying the biggest thing that we learned about autism is it's it's genes. It's just if there's a spectrum. And if you were, I would gather that if you were to get, you know, parents of a like, you know, an autistic child teen or whatever, and you said, hey, there's something that we could we can give them that.

00:34:17:27 - 00:34:18:11
Leslie Schlachter
I mean, that.

00:34:18:16 - 00:34:18:54
Dr. Alex Charney
That's what we do.

00:34:19:01 - 00:34:20:15
Leslie Schlachter
That's amazing.

00:34:20:20 - 00:34:46:52
Dr. Alex Charney
Yeah. So, so yeah, so we have we have a program now that does, it's built off of discoveries that were made through the Living Brain Project. So because we were able to like, I don't I don't know how much the the audience may really understand this, this, this immense challenge you have when you have made a discovery related to, like, a new drug in a mouse and how hard it is then to transmit that information to a human being, right.

00:34:46:58 - 00:35:11:57
Dr. Alex Charney
Where, like once, every single drug that gets gets developed and then first treat an animal never makes it to even be tested in humans. Or if it is test, it never makes it to actually get approved by being effective. Right. So this the ability now to use the living human brain samples as this new step to verify that the drug you've developed does influence human brain biology.

00:35:12:01 - 00:35:39:46
Dr. Alex Charney

That's a critical step. Oh yeah. Yeah. Now you've got, a new way, a new level of evidence to like when you're applying to the FDA to, like, look, this drug that we're proposing to use, it doesn't just work in animals. It actually gets into the human tissue and has the intended effect. So this opens up the ability to do things like test, and then, ultimately bring new drugs to patients with conditions like with, like autism.

00:35:40:01 - 00:35:44:00
Dr. Alex Charney
And we're actually doing that specifically for autism. And then so in schizophrenia right now.

00:35:44:15 - 00:35:56:17
Leslie Schlachter
Outside of like podcasts and things like this, how do you how do you teach the general public that, like, this is how you move the needle and how we actually eventually can treat these illnesses?

00:35:56:22 - 00:36:02:07
Dr. Brian Kopell
We we, we collect the data, we collaborate and we publish. And that's the best way we hope.

00:36:02:07 - 00:36:07:59
Leslie Schlachter
It trickles down. Yeah. You know, people these days do TikToks for stuff like this.

00:36:08:04 - 00:36:28:19
Dr. Brian Kopell
Yeah. So, you know, I think probably the italics are not that this doesn't come naturally to us to do this sort of thing. So. Right, I mean unfortunately. Right. You know, we are we are, you know, sort of not of that bent. But yeah, you're right. I mean, there's new ways to communicate to people. It's a thought to consider.

00:36:28:21 - 00:36:42:43
Dr. Brian Kopell
Yeah, you know, for sure. But, you know, the collaboration goes on. I mean, that to me, that's the most important thing. That's my my North Star. I'm it's sort of I assume it's Alex's as well. And we we continue the work.

00:36:42:48 - 00:36:49:50
Leslie Schlachter
What advice would you give to early researchers, people just starting out their career that want to follow path similar to yours?

00:36:49:55 - 00:36:57:31
Dr. Alex Charney
You know, the the advice I give is, is to is to challenge the status quo.

00:36:57:36 - 00:37:20:17
Dr. Brian Kopell

I was literally going to say the same thing and find and ideally find, find a partner or colleagues that are of that same mindset and hopefully in different disciplines than your own, so that the amalgam of your, your disciplines are greater than the whole. And that's, that's what I recommend.

00:37:20:22 - 00:37:34:34
Dr. Alex Charney
I think the, the true test of the living brain projects. Impact will be, you know, if there's some other young researcher who hears about what we do and thinks, I could see a way to do it better. Right. I agree.

00:37:34:39 - 00:37:36:07
Dr. Brian Kopell
Yeah. Yep.

00:37:36:12 - 00:37:55:33
Leslie Schlachter
One of the things that frustrates me a lot about what you do is the percentage of patients that actually get the care that they need from you, right. So for us we take care of patients that have tumors and aneurysms. And I like they're literally running. They can't wait for their appointment to come in. And they want the tumor out of their head.

00:37:55:33 - 00:38:03:51
Leslie Schlachter
They want their aneurysm clipped. But a statistic that I don't love for what you do is only about 3% of patients that need your treatment are actually getting it.

00:38:03:55 - 00:38:04:24
Dr. Brian Kopell
Yeah.

00:38:04:24 - 00:38:08:57
Leslie Schlachter
So like, how do we get them in the door to you. And then to participate in a project like this.

00:38:09:01 - 00:38:31:46
Dr. Brian Kopell
You know, it's it's the notion, you know, in, in surgical procedures, there's this, sort of, definition between elective and emergent and emergent is like anything that's going to kill you right this second. And we have there is no debate about it. You either do this operation right at this moment or you're going to lose life or limb.

00:38:31:46 - 00:38:49:17
Dr. Brian Kopell
Right? Yeah. And then there's everything else is called elective. Yeah, but the elective stuff, like taking a brain tumor out in a planned way is considered elective. It's elective. But is it really? In other words, who's going to elect to literally keep their brain tumor.

00:38:49:17 - 00:38:50:20
Leslie Schlachter
Right. So many people actually.

00:38:50:27 - 00:39:32:31
Dr. Brian Kopell
Well, but but right. But like you you understand what I'm saying and I do I do like and so the, the stuff that I do is almost truly in the, in the essence of elective, in the sense that there are so many other treatments that these patients are presented with, that the notion of undergoing neurosurgery becomes a much more daunting issue, and it's only daunting because there we have failed as a field to really sort of express the grand improvements in quality of life of this approach to just medications alone.

00:39:32:36 - 00:39:41:07
Dr. Brian Kopell
And that's not a failure of the patient's understanding. I would put that failure on us as a field that we have.

00:39:41:18 - 00:39:43:33
Leslie Schlachter
The treating neurologists need to really know.

00:39:43:36 - 00:40:01:36
Dr. Brian Kopell
And I mean the field, I mean neurosurgeons, biologists like all of us together, have not been able to truly communicate the impact of quality of life on this. You know, this type of procedure on patients lives. And, you know, we just got to do better.

00:40:01:40 - 00:40:06:01
Leslie Schlachter
To be really clear about what he's saying and add in. Yeah. Diagnoses.

00:40:06:05 - 00:40:06:38
Dr. Brian Kopell
Yeah.

00:40:06:43 - 00:40:48:55
Leslie Schlachter
Doctor Koeppel is a neurosurgeon who specializes in a treatment called deep brain stimulation, DBS. And historically and still, there is patients out there who have Parkinson's. And in Parkinson's, you can have a tremor. For many patients, they're treated by their neurologist. There's medication. Some don't even get the appropriate medications. But if people have such bad tremor that it's affecting their life, meaning they can't even pick up a pen or give themself water, there's a procedure that they can do called deep brain stimulation, where neurosurgical electrodes are put into the brain and stimulate a part of the brain that calms the tremor, either cures it or diminishes it enough that they have improvement in their

00:40:48:55 - 00:41:14:09

Leslie Schlachter
life. And so the statistics are there's only about 3% of patients out there that are actually getting this treatment that could benefit from it, which is a crazy number, like that's 97% failure. So if you know someone that has Parkinson's, they don't even need to even have that bad of a tremor yet, right? Like to get into doctors that know how to take them down the path and part and tremor with Parkinson's is just one thing.

00:41:14:09 - 00:41:21:46
Dr. Brian Kopell
Yeah. I mean, you know, the truth is, is like, you know, the mainstay of Parkinson's therapy. I'm going to say something pretty controversial. I probably get.

00:41:21:46 - 00:41:22:49
Leslie Schlachter
Yeah. Love it. Let's do.

00:41:22:49 - 00:41:32:18
Dr. Brian Kopell
It. Let's do it. So the mainstay of, of of Parkinson's treatment is the replenishment of dopamine. Right. That's the that's the fundamental original. We all.

00:41:32:18 - 00:41:32:51
Leslie Schlachter
Agree on that.

00:41:32:52 - 00:41:55:19
Dr. Brian Kopell
Of, of of of of Parkinson's is that your dopamine producing cells die. And so we have to give back dopamine. Well, the truth is, you know, we do that by giving either pills or pumps or so on. But the way that the brain organizes its own dopamine use is very, very specifically at contextually appropriate moments. We don't have the ability to do that.

00:41:55:19 - 00:42:24:03
Dr. Brian Kopell
So we just give you a giant swat, you know, wave of dopamine that you're just getting on a daily basis and early on in the disease, that's fine. But, you know, more and more that we're beginning to see is that over the long period of time when you mess with the dopamine system, and we all know this based on social media and things of that nature, is that your dopamine system gets dysregulated and that that is the essence of the quality of your life.

00:42:24:03 - 00:42:34:51
Dr. Brian Kopell
Right? Dopamine is our reward mechanism. It's, it's it's what allows us to pursue difficult things. And if that becomes deranged, then your quality of life is decimated.

00:42:34:53 - 00:42:35:12

Leslie Schlachter
Right.

00:42:35:13 - 00:42:58:43
Dr. Brian Kopell
One of the great things about deep brain stimulation is that it allows us to sort of mitigate that wave of dopamine replacement and still maintain your motoric benefit, so that you can move and do your life and have all the quality of life. But we're minimizing this, a physiologic, you know, replenishment of dopamine. And that has an implication in terms of the quality of life.

00:42:58:48 - 00:43:26:18
Dr. Brian Kopell
One more thing, as well, what happens when patients get advanced Parkinson's disease? They stop exercising. They stop eating protein because the protein interferes with their medication. So you begin to sort of do things in your life that actually hurt your longevity, right? If we can intervene DBS much earlier, then we can avoid those behaviors that really are going to actually impact your long.

00:43:26:19 - 00:43:28:16
Leslie Schlachter
And maybe future gene therapy.

00:43:28:21 - 00:43:30:24
Dr. Alex Charney
There. Definitely.

00:43:30:28 - 00:43:43:00
Leslie Schlachter
So we talk about a lot today. There's like this overlap of neurology, psychiatry, neurosurgery, neuroscience. What would you say is the biggest bit of misinformation in your field specifically? You guys will each take a turn it?

00:43:43:04 - 00:44:06:34
Dr. Alex Charney
Well, I'll talk specifically about people who have schizophrenia. Because it's an easy it's an easy answer when you can think about that because no one understands in the general public has a good understanding of what it means to be schizophrenic. You know, and, people walk by individuals on the street suffering from schizophrenia who are hearing voices that aren't there and talking to themself.

00:44:06:34 - 00:44:33:21
Dr. Alex Charney
And, you know, it's easy to brush them off as, oh, they're just crazy or they're on drugs. And these are individuals who are suffering incredibly. So I think, you know, the the general lack of understanding in the public as it relates to severe forms of mental illness, think common forms of mental illness like depression, anxiety, the public has gained a lot more sensitivity over recent years, but still, the more severe forms like psychosis, still are people.

00:44:33:21 - 00:44:43:07
Dr. Alex Charney
These individuals are ostracized and and poorly understood. And that's that's something that, I think a lot about because that's, that's my the patients that I treat and, focus on in my research.

00:44:43:12 - 00:45:11:02
Dr. Brian Kopell
The biggest misinformation is something we already just touched on, the idea that this deep brain stimulation is a is a dangerous procedure in the sense that I think that the the danger and the risk of this procedure is so over blown. And patients, of course, are going to sort of make that overblown because they're laypeople. But I think that it's not based on reality.

00:45:11:02 - 00:45:39:34
Dr. Brian Kopell
And in fact, it was recently a patient, a paper that was published, that looked at the rates of morbidity complications compared to, like a lot of commonly index procedures like C-section, for instance. And deep brain stimulation is way safer than these procedures that we typically think of. Oh, it's no big it's no big deal. Oh, it's a common procedure.

00:45:39:39 - 00:46:03:37
Dr. Brian Kopell
You know, one of the really nice things about deep brain stimulation and the fact that we've been doing it now for 30, 30, 30 years is that we do it really safely and to leave quality of life on the table in the face of that relatively safe procedure, I think is a is a huge piece of misinformation. And if we can overcome that, we'll help a lot of people.

00:46:03:37 - 00:46:04:03
Dr. Brian Kopell
Yeah.

00:46:04:08 - 00:46:13:13
Leslie Schlachter
Because it's not like for the trauma. It's not just the it's not just the tremor that you're getting rid of, like it's the ability to eat, feed themselves. Of course, it's everything's all over.

00:46:13:13 - 00:46:22:45
Dr. Brian Kopell
With all of the downstream effects that are we as a field of medicine are sometimes it's hard for us to convey that point. Right.

00:46:22:49 - 00:46:44:29
Leslie Schlachter
I have a similar situation in my in my practice, we treat a lot of patients that have trigeminal neuralgia, severe facial pain, and they come to us after they've been on, you know, months or years of medications, multiple medications. Their pain is refractory. And it's I

guess under, there's like kidney stones, trigeminal neuralgia. And then like, what's the chronic regional pain syndrome?

00:46:44:29 - 00:47:06:21
Leslie Schlachter
That's a European. Yeah. By the time they come to us, they're like, you know, begging for us to drill a hole in their head to do the surgery. And I think even then, we only treat like 20% of people that could benefit from it. So to laypeople drilling a hole in your head to fix a problem may sound crazy, but it's actually proven decades to be safe and help people.

00:47:06:21 - 00:47:27:09
Leslie Schlachter
So I will volunteer to participate in a Living Brain project. If there's a way that you can learn of what happens in my cycle when I before, during and after what those hormonal changes are, I'd love for more information on that. So when every woman ever, is there anything that you guys want to add? This was I feel like we just touched on the tip of the iceberg.

00:47:27:09 - 00:47:34:47
Leslie Schlachter
I'm very interested in this, and I and I hope people got the point from this today. But is there anything else that you guys want to add that we did not discuss?

00:47:34:52 - 00:47:37:39
Dr. Alex Charney
No. Thank you for the opportunity to talk about it. That was good.

00:47:37:44 - 00:47:39:59
Leslie Schlachter
Thank you guys so much for being here. I appreciate your time.

00:47:40:01 - 00:47:41:12
Dr. Brian Kopell
Thank you.

00:47:41:16 - 00:48:02:16
Leslie Schlachter
So that's all for this episode of The Vitals, I'm your host, Leslie Schlachter. Subscribe to the vitals and the Mount Sinai Health Systems other video podcast programing on YouTube, Apple Podcasts, Spotify or wherever you get your podcasts. To learn more about Mount Sinai Living Brain Project or to book an appointment with a mount Sinai psychiatrist, neurologist, or neurosurgeon.

00:48:02:31 - 00:48:14:13
Leslie Schlachter
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