0:01 Dr. Michael Reber
[Your Complex Brain theme music] Basically, we are trying to retrain the brain to use what's left of this healthy vision and make it more sensitive by using both vision and audition to detect element in space.

0:21 Heather
[theme music continues] This is Your Complex Brain, a podcast all about the brain, the diseases that impact it, and the path to finding cures. I'm your host, Heather Sherman, and I have the great pleasure of working alongside the team at the Krembil Brain Institute in Toronto, Canada, a leader in brain research and patient care. In each episode, we'll take you behind the scenes into our clinics and research labs to meet the game changers of the future. We'll also empower you with the latest research to help you take charge of your own health. You'll hear directly from people who are living with brain disease, as well as their loved ones and the care teams who support them. Join us on a journey to unravel the mystery of your complex brain. [theme music continues then fades out]

[gentle electronic music] Today on Your Complex Brain, we're talking about a home-grown vision rehabilitation program. The goal is to help young brain cancer survivors whose sight has been impacted by their tumours improve their vision. The program uses virtual reality to effectively retrain parts of the brain, allowing them to better perceive objects and obstacles. Jack Conway was one of the first research participants to sign up. Here is his story. [gentle electronic music fades out]

1:57 Jack Conway
[sparse, rhythmic electronic music] My name is Jack Conway. I am 18 years old. I am very passionate about politics and theme parks. So, in my family, I have my mom named Kim, I have my dad named Steve, I have an older brother named Brian who I don't see much because he's in college. So, I play video games with my friends or by myself. I play a variety of games from Call of Duty to Minecraft, and all sorts of things, so I'm able to kind of express my creative mindset in Minecraft or just kind of unleash any stress or whatever in Call of Duty, that sort of thing. I also love roller coasters; you could pull up a picture of a roller coaster and I could either name the coaster, park it's at, or both. I'm kind of a roller coaster nerd.

[light, bubbly, electronic music] When I was six months old, I was diagnosed with an optic pathway glioma brain tumour, which is a tumour that grows on the optic nerve, and that tumour, even after treatment with chemotherapy, did damage the optic nerve and, therefore, I do have a vision impairment. It's not a huge impairment, but it's a significant one where I do have trouble reading small fonts and, according to the government, I can't get a driver's license. I mean, with the way people drive, it's okay, but I do wish I had that freedom. When I was diagnosed, we did meet Dr. Bouffet, and he ended up being my neuro-oncologist for the duration of my first battle. He put me on, I believe it was a 14-month protocol of vincristine so I worked with him that whole time, and then even after I finished my first rounds of chemo and beat the tumour for the first time, I would still see him every few months for MRIs or appointments and that sort of thing.

And then, when I was re-diagnosed, I was put on vinblastine, which is a chemo treatment that he created himself, along with members of his team, and that treatment is now the number-one course of action that they will use for other children that are diagnosed with the same tumour that I had, and I was one of the first children in the world to receive that treatment. I spent my first birthday and Christmas at SickKids. I've spent time there for appointments and stuff, which, when I was on treatment, the second time would take the whole day; it would be six hours of waiting for treatment. If I added up

all the time, I've probably lived at SickKids for four years of my life in total, with all the visits and stuff combined, which is a lot of time.

[laidback electronic music] I would say, first, small text, my nose would be a couple of inches from the screen, and that would be the same at books and, in fact, with school textbooks, my nose would be pressed up against the page of the book because the font in those is very small. So, it's mostly with reading. I do have good visual observations just around in general so I can see things. Like, I can see oncoming cars or oncoming street signs, things like that. I can still make details, but when it comes to reading, that's really where I struggle. I can ride a bike, I can throw in catch a baseball, I can do all sorts of things, and I'm happy I can do that. It's just the one thing I can't do is drive a car. School can be challenging for me, specifically, because of my vision. It can be difficult to engage on certain activities. In Phys Ed, for example, I enjoy being active but when we were doing games like badminton, it was impossible for me to see the birdie. I actually couldn't play badminton because I had that inability to kind of discern the birdie from the surrounding area. Even when we tried spray painting eight different colours to help it stand out, it still didn't work. I also was limited to the teams I could partake in, especially in elementary school, because the teachers, back then, were very cautious about who they picked up on those teams, and I don't think they wanted a visually-impaired kid to be on their team because they wanted their team to succeed, and they thought that I would bring them down.

[laidback electronic music fades out] Especially, like I said, when it comes to textbooks, it can be frustrating to read small fonts. Luckily, in my classes, if I do have a textbook, it's digitized, because that's where my school is now. [chuckling lightly] Sometimes—actually, quite often—will walk by people I know and not say, "Hi" to them, because I didn't realize who they were until I was basically right next to them. I didn't pick up their facial details from a far distance. And then, when I was in a small group of friends, a few weeks ago, I would, like, walk by them and they would all laugh because they think I'm blind. [laughs] Well, I kind of am blind. It's funny. I like the jokes that people make about it.

[pensive electronic music] I first heard about the study from, I believe it was Dr. Uri Tabori from SickKids. During one of my follow ups in 2018, he did mention that a vision study was going to be conducted at Toronto Western, and other teams from SickKids involved, and we put our names on the interest list and didn't hear anything for a few years, mostly because of COVID. I think it was around summer of last year, we did find out that it was going ahead. It takes place using virtual reality goggles, so I'm aware of these virtual reality goggles on my face. They're the Oculus Quest 2 headset, I believe. There's a program in there that I would pull up. It's called Revision, I believe, and it was a black screen with a white box or, I guess, the silhouette of a box, and in the box were several balls that were yellow. And then, they would be organized at the beginning in a diamond shape, and one of them would flash red, so that would be the ball I would focus on. And then, after a few seconds, the game would start, and then they would all move around. It would start off very slowly. They would kind of move, bounce off each other, bounce off the box, that sort of thing. And then, we'd do that for about 15 seconds, and after 15 seconds, it would stop, and I had to click the ball I believed was the correct ball. [pensive electronic music fades out] And then, if I was right, it would say "correct", and if it wasn't, it would show me the correct one, and it got harder as time progressed. It took about 45 minutes in total, and it got faster as each round progressed. The speed did increase to the point where, at the very end, it was like rocks in a blender, [laughs] just bits flying all over the place.

[uplifting electronic music] I had my first appointment. They would do an eye exam and see kind of where my vision was at. And then, after two weeks of the trial, they would have me come back in to do another vision exam to see where my vision was, if there were any improvements. And then, two weeks

after that, I would go in for a third exam, and then they would do the same thing. I would do this every other day for the duration of that four-week period. We actually had it extended to six weeks; we got a two-week extension on it. At each appointment, they did find that my vision had improved slightly because of the frequency in which I did it, and just the way I was supposed to do it, which was by just using my eyes and not moving my head in any way, so I was really focusing on kind of using my peripheral vision or my central vision for it. [uplifting electronic music fades out]

I noticed that the rest of the night, after I would do it, my vision or my focus was better, my eye fatigue was less prevalent, and I did find that when I was playing my games, my accuracy in those games was definitely enhanced because of the fact that I was more focused and my peripheral vision, because it kind of got a workout, it was better, as well. [bubbly, electronic music] I think it's an incredible idea that vision can be restored using technology, as opposed to procedures and surgeries. I do get very excited about the fact that vision can be corrected using technology. With all the new tools that are being created, the fact that you can just pull up a program on a device and then use that program and that program will actually improve your quality of life is remarkable to me. I would absolutely continue to do this specific program. I think that the six-week trial could open the door for maybe a more permanent sort of habit of going on every other day and doing this. And, yeah, that takes time, but if it improves my quality of life over time, then it's worth taking that time to do that... and I enjoyed doing it. [bubbly, electronic music fades out]

10:41 Heather
[Your Complex Brain theme music] What an impressive young man. For Jack and others who are living with the effects of brain cancer, this virtual reality vision rehabilitation program has been a game changer, and it was developed right here at UHN. The research is part of a world-first study to address vision challenges in pediatric oncology patients. Today's episode is all about serendipity – what happens when a vision researcher has a chance meeting with a pediatric oncologist, and that collaboration leads to unexpected and promising results. Joining us on the podcast today is Dr. Michael Reber, a neurobiologist, and a senior scientist at UHN's Donald K. Johnson Eye Institute, and Dr. Eric Bouffet. He was past director of the Pediatric Neuro Oncology Program at the Hospital for Sick Children, and the first Garron Family Chair in Childhood Cancer Research. Thank you both so much for joining me today.

11:43 Dr. Eric Bouffet
Hi, Heather. Thank you very much for having us.

11:45 Dr. Michael Reber
It's a real pleasure to be here today. Thank you for the invitation. [[Your Complex Brain theme music fades out]

11:51 Heather
Well, stop me if you've heard this one before, okay? So, a neurobiologist and a pediatric neuro-oncologist walk into a bar. [Dr. Bouffet laughs] You haven't heard this one? Okay. I'm kidding. I'm kidding, but I bet there is a great story about how the two of you met and started working together. Dr. Reber?

12:08 Dr. Michael Reber
Well, we met because our wives worked together, so that's how we met. We didn't know each other at all, and we started to talk, and then Eric was telling me about his work and amazing experience, and I was telling him what I wanted to develop here at the Donald K. Johnson Eye Institute.

12:26 Dr. Eric Bouffet
Michael was talking about visual rehabilitation and, you know, I see, every day in my practice, kids who have visual impairments, so I was just jumping, and I said, "Let's talk about kids," and so I explained what I was doing on a daily basis, and that's how we started just to work together.

12:46 Heather
Amazing. So, we're going to get more into the collaboration, but I want you to tell me a little bit about the study that the two of you are working on together. So, you're using a pioneering vision rehab system to help, as you mentioned, Dr. Bouffet, pediatric patients with brain cancer. Can you tell me how many children were involved, and what were their specific vision challenges?

13:04 Dr. Michael Reber
So, Dr. Bouffet had a cohort of 10 patients who were treated for brain cancer. Basically, these children had vision problems and most of them had so-called visual field defects in the form of hemianopsia. So, this is a visual defect where basically half of your visual field is missing; you don't see in half of your visual field. And, you can easily imagine how this can affect your daily living and daily tasks, especially when you are 10, 12, 13, or 17 years old, and that's a time in your life which is very important, when you socialize, interact with people, play sports, but also go to school and learn. So, this dramatically affects their life.

13:53 Heather
Can you tell me a little bit more about this condition? When you say that they can't see half of the visual field, what does that look like? What can they see and what can't they see in daily life?

14:03 Dr. Michael Reber
So, in daily life, their conscious vision in this blind field is lost. So, if you have a right hemianopsia, for example, you don't see what's in your right visual field. You can still see what's in the left visual field, but you don't perceive, and you don't see, consciously, what's in the right field. Typically, patients have a hard time, you know, walking around. They bump into objects. They bump into people in their right field. So, what they do to compensate for that, and they naturally develop this type of compensation is that they turn their head and eyes more often towards this blind field, to scan it more often than they would do with their regular visual field.

14:47 Heather
It's funny. You and I had a conversation prior, and it took a while for me to kind of grasp the concept too. I was thinking, "Is it one eye? Is it peripheral vision?" So, it's kind of a little bit hard to understand.

14:57 Dr. Michael Reber
It's difficult to understand because we have binocular vision, which means that you can close one eye or the other, you still see in front of you basically the same thing. So, unlike other animals like horses, for example, who have eyes on the side, and they have a very low binocular vision, so it's a concept which is a bit difficult to grasp, indeed, because this is due to an absence of visual information processing in the back of your head, so where the visual cortex lies, and this is where the visual information is no more processed, and this is why you have either the right or the left field, which is basically blind.

15:37 Heather

And Dr. Bouffet, I wanted to ask you, how does a tumour affect vision, versus a vision illness, for example? What is specific about these patients and their condition?

15:47 Dr. Eric Bouffet
[atmospheric electronic music] There are different tumours that can affect the visual field or vision. So, some tumours grow into the optic track and now, exception, of course, but in my field, they are relatively common, so we see on average, in Toronto, between 10 and 20 patients like this per year, and particularly very young patient. When they grow into the optic tract, the threat is just directly to the vision, and if the treatment is not successful, the vision would go. But, if we can also find a treatment that will stop the deterioration of the vision, that's a success. But, you have to keep in mind that the way we diagnose these kids is because they have a visual problem. They have low vision because the damage is already here when we see the patient, first, and that's why we need some rehabilitation program.

Now, on the way, the tumour can affect the vision by pushing on the optic tract, and sometimes this push can be transient, and we can see a recovery, but sometimes we see a permanent damage, and sometimes, also, we have tumour but growing into a place of the brain where you have to remove the tumour. And, as a result, you also remove some of the optic track, and particularly when they are in the back of the brain, and this causes a permanent loss of the brain function that is integrating the information that is coming to the eye because when you see, it's a gift to see. It's phenomenal – the information goes just back within one thousandth of a second to the back of your brain and is integrated, and Michael knows much more than I know on this. [Heather chuckles] It's magic here. Every damage to this optic pathway can cause some sort of visual deficit, but hemianopia is one of the most common.

18:00 Heather
Can you tell us, Dr. Reber, more about the technology itself? How is it different from regular virtual reality? [atmospheric electronic music continues]

18:06 Dr. Michael Reber
So, this particular approach that we have been developing in the lab now for the last four years, I would say, with originally other types of patients, we were focused on patients with macular degeneration, so these are individuals who lose vision in their centre field, and they can't read anymore. [atmospheric electronic music fades out] So, this technology was developed, basically, to try to help individuals with vision loss—and then, particularly, visual field loss—to kind of train the brain to use what's left of the remaining healthy vision. So, it's basically some sort of re-adaptation, or retraining of the brain. So, the paradigm is called the 3D multiple-object tracking. What it does is that the individuals are asked to track a target into a virtual 3D environment, and this target is moving within that virtual 3D environment, and we ask them to track this target using both vision, but also sound. And, this is the important aspect of our retraining here is to use those two senses that you use on a daily basis when you walk in the street, you know? So, basically, we are trying to retrain the brain to use what's left of this healthy vision and make it more sensitive by using both vision and audition to detect elements in space.

19:41 Heather
And how can sound help with vision?

19:45 Dr. Michael Reber
Sound and vision, they all go together, and then, on a daily basis, when you walk in the street, if you wouldn't have sound, you would be in a pretty bad situation, I would say, and it's pretty dangerous. For

example, if you remember one of those hot nights during the summer, right? You are laying in your bed, it's totally dark in your room, and you can listen to these horrible mosquitos, you know, flying around you.

20:11 Heather
Oh, I hate that.

20:12 Dr. Michael Reber
You know where it is, you know? You don't see it, right? But, you know whether it's, like, more on the right side or left side or right above you or a little bit behind you. Well, this is exactly what happens on a daily basis, you know? When you walk in the street, your vision tells you that you see, for example, an incoming object from your peripheral retina, and this incoming object, if it's a truck or a car, also emits a sound. And so, the brain basically computes both the image and the sound, relative to their spatial location, and tells our brain, "Okay, this might be dangerous," you know? "Maybe you should pay attention to this incoming object because you might get hit soon if you don't pay attention to it." And, what happens is that this part of the brain, which is located, I would say, just behind the eyes, is this area that will tell your brain to orient your eyes and also your head towards this element coming towards you. So, it's really some sort of reflexive detection process, and this is what we are trying to stimulate in these patients that we have with Dr. Bouffet, is basically, we are trying to make these tiny little structure located behind the eyes, to make it more sensitive to these incoming objects so that those patients are now able to perceive incoming objects more efficiently, and therefore orient their head and eyes towards the incoming object and, in this case, for them, moving the object into the visual field, which is not affected, and therefore they can identify whether or not it's a dangerous object, for example.

The goal is really to help them to become, you know, safer or feel safer when they go out. I mean, a major issue for a patient with hemianopsia is, of course, driving, but walking around in busy places can be challenging for them because, as I said, they don't see what's happening in their blind field, and so if there is an incoming object in their blind field, coming towards them, they won't see it, so they can be easily hit. And, that's why they bump into people. That's why they bump into objects, you know? Basically, the idea is to increase their self-confidence, going around in busy places, in unfamiliar places, also – that's the main goal, and which, ultimately, will affect their quality of life.

22:43 Heather
Mm-hmm. And, their independence.

22:46 Dr. Michael Reber
Absolutely.

22:47 Heather
[gentle, upbeat electronic music] And how do you measure improvement in vision in somebody with low vision? And, can you tell me about the results? I mean, what did you find in the study?

24:01 Dr. Michael Reber
Vision is assessed using a whole set of standardized tests in ophthalmology, and this is performed by the ophthalmologists here at Toronto Western Hospital and the specialists in low vision, which are Dr. Daibert Nido and Dr. Markowitz. And so, patients are spending, basically, two hours with the ophthalmologists and go through a whole series of different tests, and what we've seen so far is that

half of our patients are positively responding to our treatment, and we see significant and strong improvement in visual field restoration, which means that these patients are now able to perceive—and I insist on the perceive because they don't see but perceive—elements in their blind field.

24:56 Heather
That's amazing – 50%. I mean, what had you expected?

24:59 Dr. Michael Reber
Well, I had really no expectation. Maybe Dr. Bouffet can answer this because, to me, it's great. [Heather chuckles] I would have loved it if it would be 100% of participants positively responding, but this seems to be a bit utopic, maybe.

25:17 Dr. Eric Bouffet
So, just to take a step back, we started this with two former patients—and this was the exciting part—the first time we did work together, it was with a patient I met when he was 7 years old, and he is now 28 years old.

25:35 Heather
Wow.

25:36 Dr. Eric Bouffet
He had a clear visual field cut, and another patient was 32 years old, and I met her when she was 14 years old. So, that's how we started. We decided to have a sort of pre-pilot experience with added patients. It was easier There was no need for ethics committees. They were just happy to participate, and it was very straightforward, and the improvement was spectacular and really, really, this was very exciting. We wrote a paper together, and this was the first paper we wrote together – very exciting as well, because I think it was very welcome and easy to publish. It was really fascinating to see that, with clear measurement, there was benefits here, and they were describing a number of benefits, including reading speed, for example, and self-confidence, able to walk faster, and things that we were not anticipating. And so, then we said, "Let's move with the kids," but we also added some complexity to the question, which is, "Now, we need to see whether the place the tumour is growing, is influencing the benefit from this device." And so, we are still looking to this, but it seems that the 50% we are seeing is related to the place the tumour has grown, so we need more, and we may need many more patients who have a better idea of who, as the respondents, the issues are certainly how long the deficit has been here, where is the tumour located, but also how compliant the patient is because, you know, we are dealing with kids. The minute they can play, they play. If they don't play, they get bored. So, there are also these issues, how we can just captivate their concentration, because it requires some work from their side.

27:52 Heather
Right? It's got to help, though, that it's virtual reality, and a lot of these kids are very familiar with the technology, and it's also remote. It's done at home.

28:00 Dr. Eric Bouffet
Yeah, absolutely. So, the beauty of this technology is that participants don't need to come to the hospital. They come once, and we do all the baseline checks and visual assessment, and then we provide them with the headset, and they go home with the headset, they hook it to their own WiFi, and each time they train, we receive data, real-time. This is all secured. I mean, it's all encrypted, and so on. Then,

we analyze the data that we obtained in real time, and so, for the next session, we fine tune, I would say, the training, based on the previous performance. [upbeat music] And so, this keeps the participant or the patient, every time, on their toes. You know, it keeps you at the edge of what you can perceive, and so this is why we believe, also, it's very efficient, because it's pushing the participant all the time, more and more, you know? So, if they improve, the next time, the task is going to be a bit more difficult. If they fail or because it's a bit too difficult, then the level of difficulty decreases on the next session. So, it really adapts to the participant's performance, and yes indeed, it's virtual reality, so it's easy for children to follow this type of treatment, I would say, because it's fun to do. You have to identify the target using a laser pointer, so it has some sort of shooting game, a little bit. We recommend they do not train past 7 or 8pm because they may have spent the whole day at school and they may be tired, so we recommend, if possible, to do it after they come back from school or maybe if they have time at noon, also. But yeah, it's very convenient because you don't have this burden of coming to the hospital every two days and perform this rehabilitation protocol, which would then probably lead to very low compliance rate. [upbeat music fades out]

29:51 Heather
Probably, yeah. Well, I've had a chance to try out the technology myself and I can say, from personal experience, it's not easy. [laughs] It is a lot of fun, but it's not easy. Dr. Bouffet, I wanted to ask you—you've been treating young patients with brain cancer for many years, and there's been a lot of advances in that time, especially in the last few years—so, what's changed in terms of treatment options, and in terms of survivability rates for a lot of the patients that you treat?

30:15 Dr. Eric Bouffet
Yeah, so if you give me two hours to answer this question, that's basically, we call these times the molecular era, so which is we can identify the idea of brain tumour now, when it was virtually impossible 15 or 20 years ago. And, as a result, we can offer targeted treatment, which is a treatment that specifically will target a mutation or an alteration in the gene of the tumour, when in the past, we're just giving, you know, bazooka medicine, which is just chemotherapy, or radiotherapy. So, that's a change. We go into more sophisticated medicine. We cannot say that the treatment, there is impact, improving success rate, but the quality of the success is much better, so which means that we can see that patients are cured with a great quality of life when the person had to pay the price of the treatment, for example, radiation or aggressive surgery. We, also, are at a time where we think—and this is where I love what Michael is doing—we think of brain repair. It's not only to treat the tumour to say, "Now, the tumour is gone. You can go, You are cured." It's just to say, "Okay, come and we want to fix what has been damaged by the tumour or the treatment." And so, this is a new form of medicine and a place where, certainly, Toronto is really at the top of, you know, the list. We say, in Europe, as Barcelona or the Paris St. Germain in football, you know, things that are happening in Toronto, which are not happening elsewhere, and this is good and bad on either side. It's just good, because this is exciting. This is bad, because we have to face, you know, the skepticism or the reluctance. So, people don't want to accept that something works, which was not developed at their place. So, that's where we are, and so we have to fight with our weapon, which is scientific evidence, clinical trials, and to get grants, so that's things that we are doing with Michael.

32:35 Heather
[hip-hop-style electronic music] Well, I wanted to ask you about Jack Conway, who's a patient of yours, and we heard from him earlier in the episode about his experience. You were the one to first diagnose and treat Jack, is my understanding, so you've really seen him through his entire journey. So, could you tell me a little bit about how he responded in the study, and how it's really improved his quality of life?

32:54 Dr. Eric Bouffet
Jack and his parents, we had a very good interaction from the get-go, and I remember I told him—when we met, Jack was one year old, so he was just a baby—I said, "Okay, we are not going to fix this in one shot." I have seen Jack for years and years and years. He got through treatment with chemo. Jack had a great response to chemo, on the two occasion. But, as a result, he has certainly a low vision. In fact, he was born probably with low vision, and the question is always here. [hip-hop-style electronic music fades out] It's just, "Can you improve the vision when the damage was already here a long time ago?" And, that's one of the $1 million questions we have with Michael – "Can we fix a problem when it has been here for many years?" And, it seems that, when you look at Jack and his journey with this rehabilitation program, this gives a lot of hope because he had a great response, despite the fact that this visual alteration was present for 15 or 17 years.

34:04 Heather
What are some of the things that Jack can do more successfully now that maybe he couldn't have done before the technology?

34:10 Dr. Eric Bouffet
This is what is really wonderful with this rehabilitation program. I think it's something which is specific; you don't improve your vision by looking around. This is not how it works. Obviously, you have to train, and Jack never trained. He never had access to visual rehabilitation, so he was using his vision but, in fact, his eyes were seen shaking, they were going all over the place, and with this training program, it gave him the possibility just to develop some tools which he was unaware of and could restore some capacity that was in him, that he was not able to use.

34:55 Heather
Can you speak more specifically about Jack in terms of some of the improvements that he's seen?

35:00 Dr. Eric Bouffet
He was much more confident just to go, for example, up and down the stairs, which is very surprising because you don't expect this with this rehabilitation, but confident in the walking, and as I mentioned, perhaps his eyes were shaking, and it improved the fixation and Michael can comment on this but, you know, you learn how to focus. When you have no way to focus it, you don't have this type of rehabilitation, so all of this improves your trust and your self-confidence.

35:34 Dr. Michael Reber
But, what is important, I would like to add here, is that, well, they all go to school, right? So, going to school is, like, learning: history, math, I don't know, English, and so on, so you must be able to read and read confidently, which can be challenging for some of them. But, it's also, you know, like social life: going outside, playing sports. If you have a better feeling or appreciation of your surroundings, you also feel much more comfortable going out with your friends, you know, joking, playing whatever, football, baseball, or things like this, and this is, I believe, life changing. It's funny, though, to listen to what Jack has to say, because it corroborates what we see with, like, very basic measures of a visual function, you know, for example, contrast sensitivity, as Dr. Bouffet mentioned, or fixation stability, or field restoration also.

When you take it as a whole, you know, and you look at the big picture, you have improvement in contrast sensitivity and fixation stability. In fields altogether, you will improve your vision, you will

improve your reading speed, you will improve your mobility, you will improve, as you say, walking in crowded areas, going down stairs. For example, you know, people who have very low contrast sensitivity cannot go downstairs. Contrast sensitivity is what allows you to discern texture on a background. So, you know, walking on cobblestones, if you have low contrast sensitivity, you can't. Going down a curb side, if you have low contrast sensitivity, you can't. And, our visual rehabilitation treatment, funnily enough, is actually improving contrast sensitivity in all different types of patients that we have been testing so far, and this includes patients with macular degeneration, so that's a whole other story. But, this seems to be some sort of a common, basic feature that is improved with this treatment, and this basic feature—contrast sensitivity—improves your life, dramatically, afterwards.

37:37 Heather
It's amazing. You're learning a lot. I mean, how could this potentially be applied for other vision illnesses or other conditions?

37:44 Dr. Michael Reber
Yeah. No, absolutely. I mean, we also learn as we do more, you know? We collect more results, so we see how they perform. Now, we recently started to collect data about eye tracking in some of the patients and this teaches you and shows us, you know, what's the strategy that these participants, now, are using after the training to perceive what's going on in their blind field. And, these are brand-new data for us, and I think for the field, and we are trying to wrap our head around it and trying to interpret and analyze this data. [gentle, electronic music] But, I think it's opening new avenues, you know, so how to make this treatment even better, because when you know how the patient proceeds to track the target and you understand how, based on eye movement and head movement, how they perform, then you can make those treatments even more specific, you know, and even more challenging, for example, for certain aspects of their vision, and maybe more efficient then, and maybe we can increase this number of positively responding patients.

39:00 Heather
Dr. Bouffet, how excited are you about the promise of this technology?

39:04 Dr. Eric Bouffet
I see already the device going around the world, and it's my dream to make it accessible to all children who have this visual impairment, but not only children, maybe adults, and to see if this can be used in other conditions because, if it works in kids with brain tumours, there is no reason that it doesn't work in kids with strokes, kids with other iteration of the vision. So, it's really something which is really exciting. It's the beginning, but not the end.

39:40 Heather
Dr. Bouffet, you're a scientist, you're also a doctor, but your research generally focuses on cancer, as you mentioned. So, what made you want to branch out and work with Dr. Reber in this area that's a little bit less familiar? I'm curious if it really was just serendipity, the two of you meeting, out at dinner with your wives. [chuckles]

39:57 Dr. Eric Bouffet
We like to spend time together. First, it's clear, but this has been the sort of click between us, but it's also because I'm very, very interested in brain repair, so I'm working with a number of people at SickKids and in other places just to see how we can fix the damage that has been caused by the tumour and the treatment. So, I have a great colleague, Donald Mabbott. We work with him. We have done exciting

work on exercise, on Metformin, and so this is a natural evolution, so looking at how we can, you know, repair visual damage was just part of my area of interest.

40:39 Dr. Michael Reber
You know, nowadays, doctors, but also patients are concerned about what's happening after, you know. As Dr. Bouffet mentioned, yes, okay, you can maybe reduce the tumour, resect the tumours through surgery, but what's next? You know, that there has been damaged there. How are these damages affecting your daily life is to be considered, also. Once you mitigate the symptoms and the effect of the disease itself, what's next, you know? Are you leaving the patients like that, and they go back home, and they continue to suffer from the consequences of this disease? Or, are we trying to help and find new approaches and new technologies to help them cope with it, or even, one can say, maybe one day fix these issues?

41:26 Heather
Right, and that's exactly what you're doing here. So, I'm just curious. Dr. Reber, as a neurobiologist, you're a basic researcher, you spend a lot of time in the lab, a lot of time travelling too, but a lot of time in the lab. You don't often get to see, you know, these clinical benefits to patients, up close, so what does that feel like to see some of the improvements that some of the patients in the study have experienced?

41:46 Dr. Michael Reber
For me, it was eye opening, sort of, you know, because we, indeed, are a little bit considered sometimes like lab rats. You know, we work at the bench all the time, eyes are glued to the microscope or to the computer to do computational modelling and so on, and you rarely interact with patients and listen to their complaints and to their daily life. I've been working in the field for 20 years, I understand a little bit about vision and how it works, and trying to put this knowledge together and say, "Okay, how can I help?" you know? "How can I potentially help those patients?" And so, you feel like you're more useful, I would say. You see a direct consequence of the knowledge that you've acquired over the years, and that you build your knowledge, and then you translate it. You move it to the medical field with the help of ophthalmologists first, also. You really need to mention Dr. Nido and Dr. Markovitz who have been of a great help by, you know, like translating, basically, what are the needs of those low-vision patients, and what I, with my knowledge as a basic scientist, I could bring into this field, and other people like like Dr. Bouffet, of course, but also other colleagues that now we are starting to collaborate here at the Donald K. Johnson Institute, with collaboration with the Concussion Centre with Dr. Taylor and Tartaglia where, again, we will be looking at, you know, what's going on in vision in those participants and patients, or what's happening after concussion, and try to develop more advanced strategies to boost diagnoses, but also help treating the consequence of a concussion.

43:29 Heather
[up-tempo, rhythmic electronic music] So, Dr. Bouffet, I understand that your collaboration extends to triathlons as well, with Dr. Reber. Can you tell me a little bit about that?

43:38 Dr. Eric Bouffet
Yeah. No, you know, I'm a bit older than Michael, but I was, at the time, I was thinking of slowing down and I did triathlon a long time ago. I haven't done it for many years, but he talked to me about triathlon and it's a passion, and finally, just he convinced me to participate in the triathlon, last year in September. This was my first triathlon in 30 years, but I really, really loved it and I think I got the bug again. So, we are going to have a season of triathlon this year. He's a great swimmer. He's a fantastic

swimmer. I'm more a runner, and we are both good cyclists. So, our dream is to win in our age category, which I think we should be able to do. We are very competitive. We are crazy competitors, both. [up-tempo, rhythmic electronic music fades out]

44:32 Heather
Which, I guess, helps in your collaboration on this study, as well.

44:36 Dr. Eric Bouffet
Exactly. You know, it's the same stamina and we enjoy it. So, when we meet, we talk about vision, but we talk about sport and triathlon, and we are already just trying to book our spot for the Paris Olympic Games. The beauty is when you have a French background and a Canadian life, you can support both nations, so it's just you double your chance of winning, so it's even greater.

45:03 Heather
It's the best of all worlds.

45:05 Dr. Michael Reber
[chuckles] It's super fun. As we talked about science, we talked about sport, and so he joined training last summer. We did one triathlon together, the Lakeside Triathlon, here in Ontario, and we have a lot of fun.

45:25 Dr. Michael Reber
We just recently applied to CHR Corp for a bigger study involving children throughout Canada, as a follow-up of the study that we've been talking about. Yeah, I think it makes communication easier and trust easier. I don't know.

45:43 Heather
Well, this is fascinating research and really promising results, so thank you so much for taking the time to talk to me today.

45:49 Dr. Michael Reber
Thank you very much for having me and Dr. Bouffet.

45:52 Dr. Eric Bouffet
It was a pleasure. Thank you for the invitation. [gentle electronic music fades out]

46:09 Heather
[Your Complex Brain theme music] Thank you to Dr. Michael Reber and to Dr. Eric Bouffet for joining me on the podcast today. Thanks also to Jack Conway for sharing his inspiring story. If you'd like to hear more of Jack's interview, please go to our website uhn.ca/krembil.

This episode of Your Complex Brain was produced by Jessica Schmidt. Our executive producer is Carley McPherson. Thanks also to Dr. Amy Ma, Twayne Pereira, Sara Yuan, Suzanne Weiss, and Megan Andheri for their production assistance. [theme music continues]

For more information about the Krembil Brain Institute, please visit uhn.ca/krembil, and you can reach us by email at krembil@uhnresearch.ca, but please note that, due to privacy regulations, we cannot

answer any personal health questions. Thanks for listening. We'll be back in two weeks with another exciting episode. Have a great day. [Your Complex Brain theme music fades out]