Behind the Breakthrough Podcast - University Health Network

Season 4 - Dr. Michael Reber

Transcript

BTB

This is Behind the Breakthrough, the podcast all about groundbreaking medical research and the people behind it at Toronto's University Health Network, Canada's largest research and teaching hospital. I'm your host Christine Coté. And joining us on the podcast today, Dr. Michael Reber. Award winning senior scientist at UHN's Donald K. Johnson Eye Institute, part of the Krembil Research Institute. Dr. Reber is a world renowned neurobiologist whose research focus includes mapping the connections between the eye and the brain, and restoring vision by retraining the brain using virtual reality. Dr. Michael Reber, welcome to Behind the Breakthrough.

DR. MICHAEL REBER

Hello, Christian. Hello, everyone. Thank you very much for inviting me.

BTB

Michael, let's start with a big part of your research pursuit over the years has been to map the networking between the eye and the brain. Let's start with why and what will that tell you?

DR. MICHAEL REBER

Well visual information reaches the brain through the optic nerve. And this is the only way visual information is conveyed to the brain. So where and how this optic nerve connects in the brain becomes essential to understand how the visual system works. So in my lab, our goal is to identify the mechanisms and organizational principle that control the development of these connections. And knowing that these connections form an extremely complex and precisely organized network that we called neural maps. And so we particularly focus on how the space around us is represented in the brain, and how we localize an object in space using vision.

BTB

Okay, so when we talk about mapping, this isn't like a roadmap of the neural networks connecting the brain to the eye, but a virtual map using computational modeling. So can you explain that to us how that works?

DR. MICHAEL REBER

Yeah, of course, I mean, a computational model, by definition, is in some sort of an approximation of what happens in reality. So competition and model is made of mathematical formulation, and complex equations that are relevant to biological parameters. And these are all encoded into a so called algorithm. And this is what the computer is running. And basically, the computer is trying to solve those complex equations. And by doing so the computer comes with the solution. And then we look at the solution. And we try to see whether this fits with real life with real observation in vivo. So in our case, our models simulates but also predicts how those visual maps are formed and organized in the brain. And this is based on well characterized and well established mechanisms, and biological parameters that we use to run this program. But this is based on on our work, but not only our work, the field is pretty vast. And we include data from our colleagues from other lab throughout the world. And we somehow summarize all those data in this mechanistic data, I would say, in this computational model.

BTB

And let's drill down a little further talk to us about the three step process you use to gather this information?

DR. MICHAEL REBER

Yeah, so we call it three step map alignment algorithm, because it simulates the three biological steps that are basically required for the formation of the of a visual map. And so these steps occur during development when those visual connections are formed in your brain. And these three steps control the formation, but more importantly, the layout of these maps of these visual maps in your brain. So the first step is the connection from the eye to the retina. So it's this connection of the optic nerve, to the brain and to specific areas in the brain. Then the second step that our lab has worked on, and discovered recently is that this projection, this connection from the eye to the brain, carry or shuffle some molecules up to the brain, they bring molecules up to the brain. And those molecules for the search step are required. So that the other cells that are connecting, know where they have to connect and where they have to go. So it's basically like a signpost, you know, that are telling other cells, okay, you can connect with this guy, and you should connect with the other guy. And this is how you set up such a complex network because you have to have very precise connections. Otherwise, if it's miswired, you're getting the wrong info, you're processing the wrong info. And you don't want that.

BTB

And I understand. So with this computational modeling that you've done, you were actually the first to construct the makeup of the molecular and cellular mechanisms of visual connectivity in the brain. Talk to us about what you found there?

DR. MICHAEL REBER

Well, we showed that this organizational principle of visual map relies on very specific genes and molecules, but also on brain activity and also some sort of competition between neurons for innovating those specific brain areas. And this whole network also functions because of a feedback loop which

modulates the activity of the brain. So what it means that is, the eye is processing a certain information, and it's sent to the brain, and it starts to be processed and elaborate and integrated in the brain. But in some of those areas, there is some sort of a feedback loop. That is basically telling Yes, you are processing the right information. Or Yes, you are on a timescale or on a location in space, you are processing the correct information. And this is very important for your efficiency to detect an element in your visual field. And also, more importantly, requires the integration of multiple senses. And in humans, especially vision and audition. So they work together for you to detect a new element in space. And I like to use these analogy, you know, for example, when you walk in the street, and you have a plane flying above you, you detect it right away, you're very good at detecting because not only you see it, but you hear it and the sound and the image are basically correlated in space, they come from the same area in space.

DR. MICHAEL REBER

Now, if you would remove the sound, it would be much more complex. And if you remove the visual information, it also becomes complex. And you have an example of this when, during a hot several nights, you are lying in your bed, and it's all dark in your home and you have this mosquito flying around, you can locate it approximately right, you know what it is…

BTB

That's the …

DR. MICHAEL REBER

Yeah, but you're never going to catch it, right. So to catch it, you have to turn on the light and see it. So this is exactly what happens when you combine both vision and audition, you are very good and very efficient at detecting things in space. If you only have one of the senses, it's becoming a little bit more challenging.

BTB

So help us then understand the potential here, Michael, in terms of translation to one day being something that could benefit patients?

DR. MICHAEL REBER

Well, understanding in this case, how the system is built and functions normally, when you are healthy, is required to understand what's going on when something is wrong, you know, you must be able to identify what is wrong. But to be able to do this, you need to know how it works normally, right so you can diagnose any disease if you don't know how the system works in a in a healthy context. And this is I would say some sort of general paradigm in biology, you know, you first need to understand the system. And that's why we have basic and fundamental research going on, because you need to

understand how it works normally to then explore a little bit further what's going on when you have a disease.

DR. MICHAEL REBER

So what we hope with this model in the future is that by modifying some of our biological parameters in this model, we might be able to mimic a dysfunction, to mimic what a disease can do. And then we can predict the outcome in terms of organization of the visual system connectivity or whatsoever, especially as we know that the brain very often is trying to compensate when there is a defect or an impairment somewhere, the brain has the ability to compensate, to a certain extent, the lack of information or the impaired information coming into the brain.

BTB

I'm curious how you measure the accuracy of your modeling in this case?

DR. MICHAEL REBER

The way we do this is when we run the model, and we obtain a solution about a specific organization of a visual system, we then go to in vivo data in our laboratory models, and see whether the model was right or not, because we have the ability to investigate how these network are organized in our laboratory models. And then we compare it with what the computational model is offering us as a solution, there is this constant crosstalk between in vivo biological observation and the model and then we can modify some of the parameters in the model so that it fits closer or better to what we observe in vivo.

BTB

And do you have a sense of how far you are in completing this mapping process?

DR. MICHAEL REBER

Well for now, I would say the the algorithm is quite good in predicting and simulating normal development, normal formation of the sensory maps of the of the visual map sorry, including the natural variability, you know, and then, every visual map you and me have grossly the same visual map but if you look at the details that will be different. So there are similarities but they are not identical. So our computational model takes that into account and is able to generate maps which differ slightly, which is what we observe in our models in vivo models.

DR. MICHAEL REBER

However, what it cannot do yet is predict what diseases, what the effect of a disease can have, or the impact of a disease on this connectivity. So this model is not yet able to do this. And so we are working on that aspects together with our colleagues here at the Donald K. Johnson Eye Institute who also work

on specific eye diseases and collect data. First, to see in vivo, how it looks like you know what's going on in a laboratory model of those diseases, what's happening in terms of circuitry and visual map organization. And then we try to implement this into our model and modify biological parameters. Because sometimes we don't know the importance of this parameter. So relative to the other parameter, for example, so we need to adjust this. So it's mostly fine tuning the model that will allow us to predict what's going on when you have a disease.

BTB

Alright Michael, what else have you and your team discovered in this mapping process of the neural envision network connection?

DR. MICHAEL REBER

Working on this, what we discovered is a more general rule that showed us that everything is interconnected. So nothing works in isolation, you know, I mean, your senses, generally speaking, all work together. So if you modify one parameter that alters the map, for example, the visual map in the brain, this will also affect other senses. And this is something that's seen and observed also in some of the patients. And so yeah, it tells you, everything works together. I mean, we have one only, and our brain areas are not working independently of one another, but they are all interconnected.

BTB

Talk to us about the reaction from the world of science to your papers on this subject in terms of virtual mapping using computational modeling?

DR. MICHAEL REBER

Well computational modeling and trying to come up with a theoretical assumption on how visual maps are formed is something that has been around for decades. I mean, I believe the first few models came up late 50s, or early 60s. At that time, it was purely theoretical, because the biological data were missing. And there were not a lot of biological data available to the scientific community to somehow implement them into those models. However, those models have really been pioneering in terms of, you know, theoretical concept of how sensory maps and visual maps in particular, can be formed in the brain. And so, as soon as the biology became available, as soon as more and more biological data and relevant biological parameters were published, people in the field started to build those models. And they are in the 70s 80s 90s, there were like plenty of models that were built and tested, with their limitation, and some of them had like very strong limitation because of assumptions that turned out to be wrong at the beginning. And the biology showed them that those assumptions were wrong, therefore, the model is invalid.

DR. MICHAEL REBER

In our case, we started from basically only biological data. So we had no pre assumption, I would say when we built the model and the way it's working, and we only integrated biological data and biological parameters, which is the reason why I believe it makes it pretty robust and pretty strong. And I think it's well recognized in the field and colleagues in the field and in the scientific community. Were quite excited to see that a model was able to predict visual mapping in different laboratory models.

BTB

Alright, let's turn to another pioneering research initiative of yours. You started it back at Krembil, I believe in 2018. That's the use of the Oculus, a 3D virtual reality headset to restore vision. Take us back to the beginning. How did you connect the potential for the Oculus to help with restoring vision loss?

DR. MICHAEL REBER

Well the work with vision loss, the Oculus and going to the patients now with low vision all stems from our lab work from this computational model, and also from other people in the field? Again, we don't do this job on our own. You know, it's a community. There are a lot of people out there, lots of scientists working on this. And all together you know, when we take a step back and look at the data all together and there are very important things that can come out. And based on these few fundamental knowledge, basic knowledge acquired over the years, which explains us how information is processed by the brain, how visual information is processed by the brain, what type of information is processed, but by what type of brain areas. The visual system is very complex and you have multiple visual areas within your brain. And I would say, although they are all interconnected, they each deal with a specific visual features, some of them are dealing with color. Some others are dealing with movement, some others are dealing with direction. And some others are dealing with location in space.

DR. MICHAEL REBER

So we are interested in how the brain deals with location in space. And we studied these particular circuitry. And it turns out that, with the advanced technological advance, and particularly brain imaging in humans, it's been shown that those circuits and network also exist in humans. And basically, although animal models or laboratory models are sometimes not very similar to humans, the way the brain is wired is very similar. And so we were able to compare those data and see that, okay, if we understand how this works in laboratory models, and humans have a very similar wiring of the visual system, maybe we can use that knowledge to try to stimulate the visual system in certain ways. So that when you have low vision, for example, when you are unable to process given type of data, because you have an eye disease, or because you got an injury to your brain, and you have vision problems and low vision, maybe we can find a way to stimulate your vision to somehow restore some sort of perception or visual perception that is missing.

BTB

And in terms of the visual impairments, we're talking about the potentially the Oculus might help with, do you have a sense yet of which impairments they are?

DR. MICHAEL REBER

Well, for now, I mean, so we have published a couple of results now. And we are in the middle of two larger studies, where we look at visual stimulation in patients with AMD. And in children also with homonymous hemianopsia, consecutive to brain tumor. So AMD, I would say everyone knows what it is. And then what is it. And for some, if you don't know, you might know soon, but we all have family who is affected by AMD. And so this is the loss of central vision. And so basically, the center of your vision becomes black and then very difficult on a daily life, because you can't read anymore, or reading becomes very difficult. So it also impacts your mobility and your independence. So it has a dramatic impact on your life. And so we are now trying visual stimulation on those AMD patients to see whether they do better in visual perception. And the preliminary data that we have now are very encouraging. Patients tell us that they feel better, they have better visual perception. And more importantly for us that their quality of life improved. That's as a researcher, but also I'm not clinician, but I guess also for clinicians is, that's the main goal.

DR. MICHAEL REBER

The other disease is hemianopsia, homonymous hemianopsia, in this case basically, you don't see half of your visual field, whether it's left or right. And this is due to, often due to trauma or stroke, also a brain tumor, and in this particular study, we, we our patients are children with brain tumor, and we have a collaboration with SickKids, to do this. And the preliminary data that we had published in 2021, were on patients with this particular disease. And we have seen amazing improvement in those patients, they suddenly were able to perceive, and I'm saying perceive not seeing but perceive objects in their blind field, the biology behind it is a bit complex, and I am not sure I'm going to go there because it may take me like 15 or 20 minutes to to explain the system. But basically, what we are able to do is to train the brain or stimulate the brain so that it can detect again, visual elements that are in this blind field. And because they are in this blind field, and because the brain detects it, without you knowing it's a reflex system, the eyes and the brain is going to tell you to orient towards the stimuli. So even though those patients still do not really see in this half field, the brains is going to tell them move your eyes towards this element. And so they are going to bring an element which is in the blind field now in their visual field, the one that they are seeing.

DR. MICHAEL REBER

So their mobility, their independence increased a lot because now suddenly, they feel much safer, you know, going around going out in the street because the brain is again detecting those elements and telling you eyes and I would say your neck muscle to orient toward this stimulus, or this visual element. So these are for now the most of the data that we have. And we have other study coming up, we are trying to investigate the effects of these visual rehabilitation, in multiply disease just to see whether it can be beneficial for everyone. It might not be. Because for some of the diseases, it would require a specific training or a different type of training that we may need to find out. But right now with what we have, we are basically testing almost every eye disease to see whether there can be benefits or not.

BTB

Do I have it right here that the premise or the underpinning of the research in terms of testing the Oculus that you're doing is the principle of the elasticity of the brain, its ability to rewire itself?

DR. MICHAEL REBER

Yes, that's exactly it. This is known from basic research and basic studies. And it's been shown also in humans using those very elaborated and complex brain imaging techniques that I mentioned earlier, some labs in the US were able to show that upon visual stimulation, the brain or the visual system in the brain, rewires. And this is I would say, some sort of capacity that the brain has. And as I said, at the beginning, when suddenly, part of the visual information is missing, the brain doesn't really understand why suddenly information is missing. So the brain is parts of the brain that were used to receive visual information, now suddenly do not receive any information anymore.

DR. MICHAEL REBER

So what happens is that the brain tries to compensate for that. And so they try to, you know, shortcut the areas that are damaged, or they, they try to make new connection, so that they can still transmit the information and the visual data from one area to the other. So this is the natural capacity of the brain, to rewire. And this is what we call in the brain plasticity or neuronal plasticity. But you can push it, you know, you can train the brain to do it in a more efficient way. So naturally, we know the brain does it. Now with our visual stimulation system in VR, we are pushing it even more. So we are forcing the brain to do this reconnection and rewiring in the way we want.

BTB

So walk us through, say for example, with AMD, what do you have the patient's doing in your research in terms of how do you utilize the Oculus and help them retrain the brain?

DR. MICHAEL REBER

I believe it's fairly easy for the patient. And I must say, we are very surprised, because AMD patients generally are older adults. So patients within AMD are generally over 70, over 80 years old. And we are kind of a bit hesitating, because VR is a new technology, right? You have to wear these headset, and this particular population is very likely not used to this technology. So we originally thought, Okay, let's do a feasible, it's so called the feasibility study, and let's say Are they at least able to use it. And it was absolutely amazing to see how this technology became familiar in less than a couple of days for these patients. They were able to all the training is performed at home. And that's also the beauty of the system is that they don't come to the clinic for rehabilitation. They come once we do all visual measurements as baseline, and then we give them the Oculus, we explain them how to use it. And then they take it home, the only thing they have to do is to connect it to their own Wi Fi at home, which when you are 85 or 90 year old might be a bit a little bit tricky. But again, we were very surprised how easy that went.

DR. MICHAEL REBER

And so they connect the Oculus to their Wi Fi, it stays there connected for basically four weeks. And each time they do a visual stimulation, we receive data right away in the lab. So we know exactly when they did training and how they performed. And then we have some sort of an algorithm running in the back in our computers. We almost call it some sort of artificial intelligence but a bit a little bit too much. But some sort of algorithm that basically is taking into account the performance and the improvement of the patient to this visual stimulation. And then for the next session, makes it a little bit more challenging. So which means that the patient never reached their limit, you know, they're challenged every single time a little bit more each time. And so what they do is basically they wear these headsets and they have to track moving targets. So they have sets of balls with yellow balls and in this particular case, they are eight balls and then one of them becomes the target and we show them which one is the target And then these target goes back to the same color of all the other eight balls. And they are supposed to track and follow these target moving in this virtual 3D space for a few seconds. And after generally 20 seconds, the whole system freezes. And using the laser pointer of the Oculus system, they must select the target.

DR. MICHAEL REBER

And if their selection is correct, the whole system moves again, but faster. And this is what I'm saying the there is some sort of algorithm in the back, that basically makes it a little bit more challenging for the next session, if you fail, if you miss the target, it slows down the speed. And so basically, over time, you'll reach some sort of an equilibrium. But over the days, you improve more and more and more. And that's what we see with patients that again, as I said, are 85 years old, so there is no age limit, to learn, and to perform better, we are quite amazed. So right now, the stimulation procedure lasts four weeks, and you train every two days, for basically 15 minutes, in the comfort of your home. They're sitting in their couch, and they do their training. And after two weeks, we asked them to come to the clinic just to have a quick visual assessment to make sure that everything is okay or so on the Oculus side, and to see whether they improve and we do this again at four weeks. And then we have follow ups at one month and six months. So I think it's also quite easy for the patients and they, and they tell us, you know, they say it's much easier than coming every day or every two days at the clinic for visual rehab, you know, and especially when you have low vision, you know, you don't want to travel every other day to take I don't know TTC or taxi or whatever, or have your spouse driving you to the hospital. This is time consuming for them. And it's stressful also.

BTB

Talk to us about the results then Michael in terms of the vision Improvement?

DR. MICHAEL REBER

We showed significant improvement in some of the basic visual function, and field vision restoration. So for example, in all those in all our patients AMD, but also the other ones that I mentioned the

homonymous hemianopsia. These patients show improvement in basic visual functions such as contrast, sensitivity, and fixation stability. So contrast sensitivity is your ability to discern texture over background, to discern an object over the background. And individuals with low contrast sensitivity have a hard time going downstairs, for example, have a very hard time going down curb sides, you know, also, for example, when you exit an elevator, you know, you have this aluminum rail in the middle, a lot of people having low contrast very often make a big step above this because they can't discern this rail. And so they believe it's kind of a big step when it's totally flat. So when you are better and you improve your contrast sensitivity, this means that you can go downstairs again that you can walk in the street, cobblestones, things like this much more safely.

DR. MICHAEL REBER

The other basic parameter is fixation stability, we show improvement in fixation stability. So fixation stability is basically your ability to fixate a point. And this is very important when you read, okay, when you're reading, you must be able to fixate the words and move along the lines. So you must have a very good ocular motor control. And so some of those patients have very low fixation stability, meaning that their eyes are moving around, and they can't fixate steadily a point. And if you can't, and if you have bad fixation stability, you can't read, you can recognize faces anymore. So those patients all have improvements in fixation stability, and we see it in another test directly related to this, which is reading speed, we have a test where we measure reading speed, and it's directly correlate it to fixation stability, and contrast sensitivity also.

DR. MICHAEL REBER

And we see that, you know, reading speed, which is on average, something around 200 words 180, 200 words, some of those patients barely reach 100. And then suddenly after the treatment they reach 150-160. So they are not back to normal. But I mean, there is a significant improvement. And they tell us, you know, we have a questionnaire, that quality of life questionnaire, and quality of vision questionnaire. And for for this particular population reading is very important, you know, reading newspapers is they've been doing this for 60 years or 50 years, you know, so that's their habits, I would say their daily reading is the newspapers and for some of them not being able to read the newspapers anymore is dramatic, effects them deeply. So they are generally very, very happy to be able to read the newspapers again.

BTB

And in terms of this research, the treatments that you're performing with the Oculus to improve vision, does it have staying power, or would they have to continue using the Oculus over time?

DR. MICHAEL REBER

So for now, we don't really know. But we have preliminary data that tell us that it's stable for at least two to three months after the treatment. Now, we are investigating this over a one year period. What I believe is that you would go through a hardcore training for like four weeks or six weeks every two

days. And then I would say, once a year, just to maintain the benefits, you go for a couple of weeks training or a week training, this needs to be still investigated. But I believe that's the idea behind it. That once a year, you will just go through that rehab process and visual stimulation process just to maintain the benefits that you acquired from the original training.

BTB

And you see, I'm just curious, are there any other applications for the use of the Oculus in terms of visual research?

DR. MICHAEL REBER

To me there is almost an infinite possibilities out there. I mean, the technology every two or three years, there are improvement in this technology coming out. For example, we are expecting October this year that a new model will come out, which includes eye tracking, built in eye tracking, which for us as scientist will be extremely helpful to understand what's the strategy the patient used to track object in their environment in their virtual environment. For now, the Oculus, for example, is recording head movement. So we know when the patients are at home, whether they move their head when they track the target. And we know that in real time, I think that's just amazing. Now what we will know also in real time is that how they use their eye movement do they track by moving their eyes and their head, both or only one? We don't know yet. But so these are the options, other options are also that you can build whatever you want in these virtual reality headsets.

DR. MICHAEL REBER

So there has been an interesting discussion going on a few years ago, when some of the people, or some patients are saying that they see better, or they feel better. But the tests that have ophthalmologist use in the clinic, which were designed originally to diagnose diseases, for some of them, they don't catch these improvement, they are not made to catch visual improvement, in a sense, related to a real world situation. So talking with some of the ophthalmologist and patient, we thought that okay, maybe we should come up with new tests, new visual tests that are addressing these real world situation. So right now in the lab, besides this visual rehab development, we also started to develop new visual tests, which are more relevant for real life. So basically, what we are doing is that we are including 360 degree videos of real life situation. For example, we spend some time this summer shooting videos around Toronto in different areas, for example, like, you know, busy intersections or quiet parks, or shopping malls. And we put those videos in the VR, and then we create some artificial disturbance to the scenery, to see whether the patient detects it.

DR. MICHAEL REBER

And this would correspond to a real life situation, when you are standing at an intersection and you want to cross this intersection, and the bike is coming, or a big truck is coming. You can hear it, and you can see it, but you're not going to cross of course, okay, you're going to stay and wait on the curbside. So we basically recreate this, because this is what the patients are telling us. They feel safer,

to go out and walk in the street and walk in busy areas after our training, but we have no real, objective way to measure it. So we are developing those new tests in the VR, of course, they will need validation and so on and so on. So it's still going to take a little bit of time. But we have strong support from the ophthalmologist, of course also from the patient, and we believe this would be in complement to the existing tests in ophthalmology very important to somehow evaluate and assess real life function after rehabilitation.

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You're listening to Behind the Breakthrough, the podcast all about groundbreaking medical research and the people behind it at Toronto's University Health Network, Canada's largest research and teaching hospital. I'm your host, Christine Coté. And on this episode, we're speaking with Dr. Michael Reber. Award winning senior scientist at UHN's Donald K. Johnson Eye Institute, and that's part of the Krembil Research Institute. Dr. Reber is a world renowned neurobiologist whose research goal is to map the connections between the eye and the brain. And he is pioneering the field of testing virtual reality to restore vision.

BTB

Now, Michael, you were born and raised in Strasbourg, France in a working class neighborhood. You did well in your science studies through high school but you were drawn more to sports, the triathlon, I understand and music where you played the drums. So when decision time came for you about what to do after high school, I understand it was some advice from your mom that inspired your career path. Talk to us about what she said to you and how you reacted?

DR. MICHAEL REBER

Well as you know at that time, and it was some time ago, the proportion of people going to university or following post secondary studies was low, especially in low income working class families. So for us, accessing university and going to university was a way to escape low income class and do better in life. So my mother has pushed us and I say us because I have two sisters that, who also went to university. And yeah, my mother pushed us to go to university. But as I said, and as you mentioned, that originally, I wanted to be a musician, originally. A professional musician, I wanted to be a professional piano player. This is probably because, as a kid, I got a chance to go to a classic concert one and I saw that pianist player all alone on stage with this nice black tuxedo, and the grand piano. And I guess I found that that was very impressive. So I said, my to my mom, I wanted to do that. And so they said, Okay, let's give it a try. So they gave me a chance to have a piano teacher for a couple of months. And after two months, the piano teacher told me, okay, do you really want to be a professional piano player? Because if I were you, I would consider exploring other options. So that was it that was it for the piano. I explored the drumming and I still do it as a hobby. So I play some kind of music, but not the piano.

BTB

Okay, so your parents couldn't afford you to send you university, but you qualify for French government funding to be able to pursue higher education. So at just 17 you leave for Paris and the Sorbonne take us back to that day that you embark on this journey, you know, leaving home, your parents, what's your mindset?

DR. MICHAEL REBER

When you're 17, I guess you want to go out and discover the world. But I was given a chance by the French government to go to university because I had good scores in high school. And so the French government has this program for low income family that they basically pay for your university years up to master. But the deal is that, okay, they pay for you. But you have to pass, you can't fail. If you fail a year, you're done. And they're not going to pay again, which puts a little bit pressure, I would say, especially when you are 17 or 18, you're not really ready for that. But I think it's a good way to start life, I believe a little bit. So, and then I chose to go to Paris, because now Sorbonne University, which at that time was also called Sud University was one of the best science universities in France. And so they offered me a spot.

DR. MICHAEL REBER

So you know, and then you are from Strasbourg, which is 500k, from Paris, and you have the most famous university and Science University in France, almost offering you a spot. And because you did good at high school, you get a chance to have a fellowship from the French government. What would you say, no? And then of course, you you take this opportunity, and you go. So basically, I spent roughly a bit over 10 years in Paris, because I did my PhD also in Paris. At the beginning, I had to work after hours after classes to afford living in Paris, because that's can become quite expensive. But this is also you know, common. Nowadays, a lot of students have extra jobs, you know, to to afford the cost of living. So that was already the case. I don't know, 25 or 30 years ago, so. So yeah, that was it. And I was very happy there.

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I understand another source of guidance for you along the way has been mentors talk to us about the influence they had on your career trajectory?

DR. MICHAEL REBER

Mentors. Yes, I had two main mentors that influenced my career trajectory. One was very early during my university. During my second year, I believe of university, one summer, I volunteered for a month to work in a lab. And that was in Paris. And this experience was very eye opening for me. It was the first time that I was in contact with science and real scientist, I would say. And I learned a lot not only about the science, but also about the mindset, you know, the curiosity those scientists have and so my first mentor was about to retire when I when I joined him and when I met him and he was extremely inspiring for me. He was, as I said, close to retirement so 65 when we met but even at that age he was like a kid in a playground. You know, he loved science, just because it was challenging, new all the

time. Coming up with new ideas. New experiments to perform, addressing or investigating new scientific question. So that was very, very inspiring for me.

DR. MICHAEL REBER

Then my second mentor, major mentor was my supervisor, my postdoc supervisor, Dr. Greg Lemke at the Salk Institute. And I think he's still is, some sort of a mentor. We talk once in a while, and he asks how things are going in the lab and so on and every time I can catch some of his remarks, and some of his mindset, which is still helpful nowadays. So I joined his lab for my postdoctoral studies after my PhD in Paris. That was in Salk Institute in San Diego. That's where I started vision. To work on neuroscience and vision, I had no clue about vision, I have never done any neuroscience before, because my education is a molecular and human geneticists, which is pretty vague, I would say. So this allows you to work in many different fields, I could have worked in immunology also, or whatsoever. So I started neuroscience and vision in his lab. And he taught me a lot about precision, and rigor in science, you know, whether you perform your experiments, or you analyze the data, or your presents, you present the results. And one thing is every time emphasizing is that the importance lies into the details.

BTB

What's your approach to failure, because it's not something we're taught how to deal with in school?

DR. MICHAEL REBER

Very true failure can be difficult to deal with, I would say that you have to learn from your failure, not to repeat what led to failure. And it's also a tolerance to frustration, and some sort of resilience, you know, so at one point, we are all going to fail and you just have to admit it and learn from it. Be smart, and not repeat what would lead to failure.

BTB

Now, I know you work a lot in the lab, you also have contact with patients. I'm curious how you reconcile, you know, the urgency of patient need for new treatments, with the fact that science takes time?

DR. MICHAEL REBER

When I was in France, before I arrived in Canada, we had like, almost or rarely interaction with patients, because I was working in like more basic research labs, and settings. So I didn't get a chance to meet or see patients. And this happened when I arrived here, the Krembil Research Institute and The Donald K. Johnson Eye Institute. And just seeing how they can struggle, you know, on a daily basis, just coming to the hospital, meeting them down in the lobby, you know, asking them to join the sixth floor of technology services, how they struggle sometimes to find the elevator, get into the elevator, press the appropriate button. These are very simple tasks that we do without even thinking for them, it can become extremely challenging. So when you see this, you're like, oh, wow, I mean, you know,

something must be done here. So, so this is what, what motivates us, you know, I would say to move on both on the basic side, but also on the VR side.

DR. MICHAEL REBER

Now, about the urgency and the fact that science takes time. I would say that well you cannot watch the science, because it takes time, you know, to confirm your findings, to get your new discoveries validated by the peers, whether they are scientists or clinicians. And I would just go back a couple of years, we have seen so much wrongdoings in science because of the rush and the COVID pandemic. And there were paper published in prestigious journals that were retracted. Just because, you know, it was just too fast. They didn't take the time to properly give you the data to properly analyze and process the data. The reviewers might have been very careful, you know. So I would say we still need to keep in mind that science takes time, at least quality science takes time. And that's what I will stick with, definitely. Human nature is becoming more and more impatient. So you have to somehow fight this a little bit and tell people that No, science needs time.

BTB

Five years ago, you're a well established scientist in France with a successful career at the Institute of Cellular Integrative Neurosciences in Strasbourg, and you decide to uproot your life and career and family and move to Toronto and the Donald K Johnson Eye Institute. What was the attraction to uproot your family and move halfway across the world?

DR. MICHAEL REBER

I mean, the opportunity given here to to combine basic bench work, I would say with clinical work in an amazing working environment with plenty of resources. The expertise of my direct colleagues, researchers here in Eye development and disease, but also the clinicians opthamologists here at Toronto Western will take care of great diversity of ideas and conditions and patients is definitely you know, what pushed me to come over here. When I was in France as I said I was working in a like Basic Research Institute and had barely any contact with patients. The strength of the Donald K. Johnson Eye Institute here and the Krembil Institute is that they combine both, you know, basic, extremely high level basic research together with clinical science. I mean, it's one of the biggest ophthalmology service in Canada.

DR. MICHAEL REBER

So they have literally 1000s of patients. So it's a wonderful resource for us researcher who want to investigate, you know, what's going on in eye disease. And this also serves my colleagues, you know, I have my other colleagues at the Donald K' Johnson Eye Institute working on eye diseases have access to those patients also. So I think this is one of the main reason why I move now it's also maybe a natural mindset. You know, when I was 17, I left Strasbourg to Paris. 10 years later, I left Paris to San Diego. Then I went back to Strasbourg in between actually, I went back to San Diego again, for a

couple of years as a invited professor. But yeah, maybe I have this in my gene, you know, moving around, I like.

BTB
You know, I'm wondering the urgency of the need for patients in terms of improved treatments, uprooting your family, you know, to sort of start a new part of your career here in Toronto. Does that create pressure for you?

DR. MICHAEL REBER

Well, yeah, of course, it creates pressure. But I think maybe, again, I may like it, I don't know, I like challenges, probably, you know, each time I'm lining up for a new triathlon race, I have a lot of stress, because I want to perform well. And then sometimes I say, Why do I do this, but I think this is a, for me, this is a driver, maybe, you know, being challenged and pushed a little bit out of my comfort zone? I don't know, again, that's a mindset. But yeah, for sure, it's pressure, but also, you know, as you age, I would say, you become maybe a little bit more confident than you know where your limits are. So maybe you are also not going in areas where you know, you're not going to succeed or you know, you're not going to make it. So it's still challenging, but with some, like, safe home, you know, for for you to minimize uncertainty,

BTB

What gets you up in the morning and gets you gets you into the lab each day?

DR. MICHAEL REBER

The excitement of discovering something new, you know, not every day, of course, but once in a while you have new data coming in, your trainees are showing you their new results, and you sit together and try to analyze and understand what's going on, especially when it's not what you expected. So then you have to solve it, you know, to to Oh, why why why do we have those data, we weren't expecting this? What's going on, you know? Meaning that we were wrong. And so we have to rethink the entire process or rethink the entire idea or hypothesis. And I think this is exciting. I think this is what gets me up in the morning and also that, you know, down the road, this may help patients, this may help individuals with low vision, you know, we have an aging population, not only in Canada, but everywhere in the world, you know, so meaning that there will be more and more older adults out there. Meaning also that there will be more and more individuals with potentially low vision. So more and more people, probably suffering at one point in their life because of low vision. And you don't want that.

BTB

Dr. Michael Reber award winning senior scientist at UHN's, Donald K. Johnson Eye Institute, part of the Krembil Research Institute. Thank you for sharing your groundbreaking research with us and continued success.

DR. MICHAEL REBER

Thank you very much for having me.

BTB

For more on Dr. Reber's work and the podcast go to our website, www.behindthebreakthrough.ca and let us know what you think we crave your feedback. That's a wrap for this edition of Behind the Breakthrough, the podcast all about groundbreaking medical research and the people behind it at the University Health Network in Toronto, Canada's largest research and teaching hospital. I'm your host Christian Coté. Thanks for listening