

# YCBS1E9 - ChronicPain\_V3\_mixdown

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## SUMMARY KEYWORDS

patients, trigeminal neuralgia, pain, nerve, brain, MRI, neurosurgeon, face, condition, gamma knife, chronic pain, procedures, fact, blood vessel, years, people, understanding

### Heather 00:10

[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 our research labs to meet the game changers of the future, and we'll empower you with the latest research to help you take charge of your own health. You'll also hear directly from patients who are living with brain disease 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]

### Josh 01:01

[light electronic music] My name is Josh Johnston. I'm a Forest Fire Research Scientist, leading things around satellite development, and I'm a father of two, and... oh, I guess I'm 38 years old. I've had trigeminal neuralgia for about 18 years now. Before that, I was just your average, sort of, wildland firefighter, and, you know, university student in the off-season, and all that. And, one day, I was walking home from school – it was in February in Elliot Lake, actually. I just dropped to the ground right there on the sidewalk. I thought I'd been shot in the face, to be honest with you. There was no bang, but I went down hard. I didn't know what was happening – just this unbelievable pain in my face. And, as a point of strange coincidence, the local hospital happened to be right across street from the school. I made my way directly over there, and it didn't take them long to figure out what was going on and, frankly, life's never been the same ever since. With this sort of condition, there's a lot of different variations of the pain. On a 24/7 sort of basis, there's always this burning sensation. Sometimes, it's almost like a grinding feeling that covers just, generally, the bulk of the left side of my face. But, there's also these triggered, what I call, like, attacks, where it's a very vivid shock sensation that, sometimes it's localized to a single point. Sometimes, it'll crackle across the surface. What it really is, is the nerve itself is sending out the strongest pain it can, and it can be extremely disorienting. It can, literally, drop you to the ground. For people to relate to it, it's nerve pain, right? If you've ever broken a tooth and had the nerve exposed, or not quite got the right freezing when you're getting a filling fixed, or something like that, it's a very similar sort of thing. It's so sharp, and it's so potent, at times, it's hard to even understand what's going on. [music fades out] Sometimes, I don't even believe that it is a real sensation, especially once it's gone. Like, the moment it stops, you just don't believe that it could have ever been as bad as it actually was... till it comes back again, and then your memory's abruptly refreshed. [sombre music] I genuinely, at the time, in that instant, I was worried that, like, a stray bullet had hit me in the face, or like a live wire. And I mean, it didn't take long for me to realize I wasn't

bleeding. There was nothing physically, outwardly wrong. The only thing I knew, in that moment, was that I was convinced that I was about to die. And, I think you know, as somebody who previously made a living jumping out of helicopters and, you know, working some pretty rough work, I genuinely mean that statement. And, to this date, no matter how many years it's gone on for, when those intense, intense shocks hit, in that instant, it's very difficult to convince myself I'm not actually about to die. It was a difficult time for me. I did not have a family doctor for a period of almost nine years, and it's not unheard of in the north, right? And so, I primarily had to go to walk-in clinics to get anything. There were no way to see a neurologist, whatsoever. I heard a rumour of a self-referring clinic in Toronto where you could go there, and they would basically triage you right through to see a specialist, internally, and then, from there, take next steps. And so, my folks drove me down and, the first morning when I showed up there, I saw a neurologist immediately and, by the afternoon, I saw a neurosurgeon to have microvascular decompression assessed. And they put some little pillows in to lift a blood vessel off the nerve in my brain. And it worked. The MVD was quite effective in removing the major frequency of shocks. Like, we're talking 500+ of those attack moments per day. It cut the number of them dramatically. But, after about nine months, the pain started to re-emerge and, a couple of years later, we went back and re-did the MVD. But, after that, that burning pain continued to get worse. The numbness, and the whole left side of my face got quite a bit worse. I think it was almost 10 years before I went back and started looking for the potential to do something else. [gentle electronic music] I'd done well, and the MVD got me into a place where I was able to take on a whole new career. I was able to do a PhD, start to finish, which is no small feat for anybody, but definitely not something that I saw on the cards, you know, back when I was laying on the sidewalk in Elliot Lake, right? So, when I got to this stage, the amount of pain that I was in, my wife basically put a line in the sand and said, "Look, you're not as okay as you think you are," and I always trust her because, frankly, she is always right. Initially, a neurologist here in Sault Ste. Marie had referred me down to Krembil for a rhizotomy, some sort of an intervention to sever the nerve, and Dr. Hodaie, it was very interesting, the way she assessed my situation. I guess there was something about the nature of the pain that indicated that part of it was connected to the nerve damage. And so, she figured that, if they actually severed the nerve, it might actually get worse, or at least it wasn't the optimal solution. And so, she proposed this idea of, we could potentially put in nerve stimulators to, kind of, override the signal the nerve was giving, so confuse it, and instead of letting it just do what it wants to do, which is make me pay, [laughs] we can give me a remote that would allow me to make the nerve feel what I want it to feel. And, it'll never feel normal, right? But I can control it to a point now where it's like a shimmering feeling for the most part. And, again, I'm not cured, right? I mean, I'm banged up, proper, here, but I have the ability to control it. I'm not at the mercy of it. And, I would say that, you know, even a few years on, I'm still managing, probably 70, 80% of the pain just with this remote-control device, and I've never had any sort of treatment or surgical intervention, provide relief for this long before, so it's pretty incredible. [music fades out] We had progressed to a point where I wasn't driving, ever. I wasn't ever being left alone with my young kids at the time, because... well, for a lot of reasons, right? I wasn't able to focus, I wasn't able to think clearly, and, you know, you don't want your kids seeing you falling down like that, right? It scares the bejesus out of them. And, for my youngest son, it was within a year or two of him being born that I would only hold him if I was sitting down. My wife would, like, put him on my lap kind of thing. There was no way I thought I'd ever be picking him up, standing there. [gentle electronic music] I can do that now. [laughs] I don't know how to explain to folks how much that means. Outwardly, there's no trace that anything's wrong with you. Everyone sees you and you seem normal, and you're enduring an

unimaginable hell right in front of them, and they can't tell. And, your kids are sitting there wanting to play with you – you know, a two year old wants to be held, and you can't do it, and you're in your 30s, right? It's not cool. I could do that now. [music fades out] Frequently, people say that one of the major symptoms of this condition, long term, is fear because you're constantly terrified. You have no idea when it's going to come, what it's going to do this time, and you don't know what the triggers are going to be. Then, that fear just slowly eats away at you and, when it's gone, and you don't have to be afraid of your own shadow. It's amazing how complicated it can be to readjusting to being a normal person. [laughs] [mid-tempo electronic music] It was almost exactly like waking up out of a coma. This was 15 years of completely lost time, in a lot of ways. But, I very clearly was still doing things, because I wake up, and I've got a career, and I've got a family, and it's amazing. The kids love it. We've had to explain in detail to the junior kindergarten teachers why my son insists that I'm a cyborg. Robot Daddy was his superhero, and it's been good for everyone. And, I mean, the journey is not over and more curveballs are coming. That's inevitable, right? Like I said, I'm not even middle-aged yet, so there's a long ways to tread on this one, but I got to have several years with the kids when they're this young, where everything was fairly normal. And, we've trick-or-treated together and, you know, played games, and we'd go camping and things like that, and that's invaluable. You can't get that time later in life. It's happening now, and I got to have it now. [music fades out]

**Heather** 12:35

[Your Complex Brain theme music] Imagine not being able to brush your teeth, eat a sandwich, or cuddle your children because of the intense pain. That's the reality for many people like Josh Johnston who are living with trigeminal neuralgia, a chronic and unrelenting form of facial pain. A smile, a kiss, even a gust of wind can unleash a throbbing so severe, some have described it as a lightning bolt to the face. Now, imagine living with this condition for years, often decades, without a proper diagnosis. Because trigeminal neuralgia is so rare and so misunderstood, some physicians have never even heard of it. Luckily, many patients find their way to Dr. Mojgan Hodaie, a Neurosurgeon and Senior Scientist with Krembil Brain Institute, and an internationally-renowned expert in trigeminal neuralgia. Dr. Hodaie performs more procedures to treat trigeminal neuralgia than any other neurosurgeon in Canada. In fact, a recent CBC story celebrated her 1,000th surgery for this condition. But, Dr. Hodaie isn't satisfied with just treating patients. She wants to better understand where the pain originates from, and where it travels within the brain, so that she can develop new and more personalized treatment options for patients. In addition to her day job, Dr. Hodaie is the Greg Wilkins-Barrick Chair in International Surgery at UHN, Surgical Co-Director of the Joey & Toby Tanenbaum Family Gamma Knife Centre, and the Education Lead at Krembil Brain Institute, training new neurosurgeons, both in Toronto and internationally. And, she joins me today on the podcast. Nice to have you with us today, Dr. Hodaie.

**Dr. Hodaie** 14:32

Thank you so much for inviting me.

**Heather** 14:34

Well, we just heard one of your patients, Josh Johnston, talk about what it's like to live with trigeminal neuralgia. What is it like for you to hear these heart-wrenching stories from your patients?

**Dr. Hodaie 14:44**

Well, it's always difficult to listen to someone who expresses how pain affects them, because the reality is that pain is such a common human experience. But, I have to say that I'm particularly touched by the intensity that patients with trigeminal neuralgia use to describe their pain. Their descriptions really vary between a thunderbolt to the face, to just, you know, escalating from there. Some patients have described it as a sharp knife that is connected to an outlet in the wall and stabs them in the face. Some people have described it as a surge of 10,000 volts to the face, and on and on. And, if we think that these descriptions are a little bit over the top, I'll just add that I have had a few patients that have a history of cancer, and I think it's something that everyone appreciates that cancer can result in severe pain, and these patients have also had trigeminal neuralgia, and uniformly they say that their cancer pain is nothing compared with the trigeminal neuralgia pain. And, the first time I heard this, I was in disbelief myself, but it's consistent. As some of the listeners might know, this condition has been known since antiquity. And, before proper treatment was found for these patients, it was called "the suicide disease" because patients either wasted away because they could not properly eat, and that would obviously affect their life negatively, or they would actively take their own lives because this pain was just too much to bear.

**Heather 17:02**

It's just so heartbreaking. Well, let's talk a little bit about the science of trigeminal neuralgia. What do we know about what's actually happening in the brain and why the pain is so intense?

**Dr. Hodaie 17:13**

So, we all have this nerve called the trigeminal nerve because it has three branches, and this nerve allows us to feel anything that comes to our face and takes that information to the brain. So, the nerve spans the forehead, the cheek, and the jaw, and if we touch our face, if we have a sunburn, if cold wind comes to our face, all of that is information that's taken to the brain and processed accordingly. In patients with trigeminal neuralgia, there is a mixed signal of some sort that we'll get to as to what the roots of that could be. And essentially, this nerve just sort of fires on maximum, and, in an unexpected manner, keeps sending signals saying you know, "There's great danger ahead," whereas, you know, that great danger is just one trying to brush one's teeth, or as one of my patients described, you know, she was just simply trying to give her daughter a kiss, and a big jolt of pain comes into the face. So, as small as this nerve is – and in diameter, I would say it would be very generous to measure it around three or four millimetres – as small as it is, it's a very, very powerful nerve. The information, in an unusual way, goes to the brain, and it's processed as such and, of course, it's an excruciating type of pain that arrests patients on their spot. Another patient of mine gave a very good description of an instance when he had pain. It was winter in Canada, of course, and he said that he was walking outdoors and a single snowflake landed on his cheek, and this resulted in a pain so severe that he had to hold on to the lamppost for about 20 minutes before he could start walking again.

**Heather 18:57**

Oh, my gosh.

**Dr. Hodaie 18:58**

So, it's this type of, you know, very mild sensory stimuli, as we described, that results instead in an extremely intense pain. [gentle electronic music] So, through the length of medical history, eventually, it came to be understood that it was this nerve that was responsible for the pain and, in the 20th century, early part of the 20th century, it was understood that it's, in fact, the compression of this nerve, oftentimes by a blood vessel that is very, very close to the root of the nerve. And then, a neurosurgeon by the name of Jannetta, in the US, in Pittsburgh, started doing these procedures of microvascular decompression where, through microsurgery, the contact of this blood vessel with the nerve would be removed and, in fact, the patients got quite a lot better. So, this slowly started a wave of us understanding the role of this nerve, the role of the contact between the nerve and the blood vessel, and the procedures that we could do to treat them. [music continues]

**Heather** 19:59

So, what other types of treatments are available for patients with trigeminal neuralgia?

**Dr. Hodaie** 20:04

So, there is, in fact, a number of procedures that are available for surgery for these patients. So, the one that I described where we remove the contact between the nerve and the blood vessels is called microvascular decompression. [music fades out] We have a procedure whereby we deliver a tiny, but sharp, beam of radiation to the nerve, which is Gamma Knife radiosurgery, which is quite effective, as well. And, essentially, I typically break down the procedures between those that are closer to the root of the nerve, and those that are more peripheral. The nerve, in fact, can be associated with a number of pain syndromes. Some of these pain syndromes are, in fact, an evolution of trigeminal neuralgia, such that the nerve potentially can become injured, either through intervention, or by ongoing disruption of the nerve, and that sometimes results in a pain that is very difficult to treat with the procedures that I described. And, it's in those instances that we intervene with procedures such as neuromodulation where, even though the nerve is injured, we can still encourage it to think differently. [pensive electronic music] And, therefore, if we deliver the right type of stimulation to the nerve, in fact, the expression of pain or how the patient feels the pain can be affected in a positive way.

**Heather** 22:23

Well, for Josh, it certainly made a difference. Can you take us through the procedure? You're actually implanting electrodes in a patient's face under their skin?

**Dr. Hodaie** 22:31

Yeah, that's correct. So I describe this procedure as extra-cranial. We don't enter the skull, so that makes it actually quite safe. But we do it, initially, as a trial because we want to know that we're, in fact, able to modulate the field where the pain is. So, I typically start the operation with a patient being awake and I ask them to point, and I use a marker – a purple marker – and I put dots in the area where the pain is, so that I'm able to use that as a guide. I typically do this trial under general anesthesia, and replace these electrodes. The patients wake up very quickly and, essentially, they have a set of wires that are coming out of their face for roughly about a week or so, with a device that allows them to manage it. And, we use that as a test, both for us to understand what settings and what stimulation parameters are required for management of the pain, and also for patients to have the ability to discern for themselves whether this is something that is viable for them, whether it works, whether it delivers

stimulation that, in fact, they find comfortable in lessening their pain. And, together, we come up with an answer and an understanding of whether this is the right way to go or not and, if it is the right way to go, then add a second setting. We again place these electrodes. [music fades out] We run them behind the ear and down the neck, just below the collarbone where it connects to a pacemaker, just that this is not a heart pacemaker. It's a pacemaker of the brain, through the fields where the pain is felt. And patients have, essentially, a remote controller so they can adjust the device. They can dial it up, they can dial it down, and use it as they need, to manage their pain.

**Heather 24:22**

One thing we haven't discussed is the stigma around pain and chronic pain. Josh talks a little bit about this, as well, in that, from the outside, he looks perfectly healthy. People would never know, you know what he's suffering with. So, what do you want people to know about the patients that you see, and the pain that they're experiencing, even though we can't necessarily see it?

**Dr. Hodaie 24:46**

Yeah, I often say that pain is a silent disease. People, oftentimes, suffer in silence. I would go as far as to say that even the people closest to them don't quite appreciate the pain they suffer. We don't see an external representation of that pain, and that really brings us to the limitations that we have, understanding an experience that is so common for all of us humans. If I see someone that has had an accident, has a broken bone and so on, you know, has a cut and they're bleeding, you know, we have a visual representation of that injury, and we are much more able to appreciate or have a connection with what the patient is suffering. But, not when they have pain. So, these patients find themselves often going from doctor to doctor, telling them about their suffering. Sometimes, it's heard. Sometimes, it's not heard. They go to the emergency room with a terrible attack. By the time the physician comes to see them, their attack is gone. Oftentimes, the attack last seconds, and then they're there, you know, looking normal. The physician is looking at them, you know, effectively thinking, "What are you doing here?" So, these type of experiences really, as well-meant as they are, they're very difficult for patients to handle, and some of them feel that their pain is not validated. So, I think a greater understanding of what this condition is, how severe it is, what patients have to endure to get good care is really important. And, you mentioned in your introduction that, a while ago – it was actually two years ago – there was the note that I had performed my 1,000th procedure and I was speaking with a colleague overseas who was amazed that there were 1,000 patients in Canada to be operated upon. And, you know, I thought about that a little bit because I realized, the more I've looked after this condition, the more patients have come to me. These patients did not suddenly have trigeminal neuralgia. They have been sitting, waiting for, you know, this condition to be known of, and for them to be able to reach a place where they get good care. And, oftentimes, patients come to me after having had this condition upwards of 10 years, 20 years, 30 years. Like, 30 years of suffering with this pain is just unimaginable, and, you know, this just speaks as to how silent this pain is, and what difficulty people have had trying to manage this, and trying to get surgical care for it. [gentle electronic music]

**Asma 27:50**

My name is Asma Naheed, and I am currently working as a Research MRI Technologist with Krembil Brain Institute. I must say, there is no typical day for an MRI Technologist. Every day, we face new challenges and they're all different. Sometimes, challenges where the patient's having implants that we

haven't heard about, so we have to explore them to find out if this implant is okay to go in. And sometimes, we come with the patients who are, like, very claustrophobic. We don't want patient who's already stressed out with the test to be more stressed. Sometimes, these are, like, very challenging, and, like, on the spot, we have to make decisions to make tests happen. [music fades out] [laidback electronic music] Dr. Hodaie patients, [with mirth] they love her. When the patients come and they will say, "Yeah, she's so nice and she's approachable." That's what her patients say about her. And, for us as MRI technologists, I always find her very supportive. She doesn't think that, "Oh, it's only MRI technologists." She always thinks that we are part of her team. She's very sweet. [laughs] [gentle electronic music] So, we see lots of Gamma Knife patients, and most of the Gamma Knife patients, they are for trigeminal neuralgia. Some patients, they will come and we are just pre-screening them. So we run some pictures through, and then the neurosurgeons, for example, Dr. Hodaie will decide, "Is this patient a good Gamma Knife candidate or not?" Then, on the day of treatment, or day before treatment, we do MRI. There are specific MRI that we do for Gamma Knife patients is we are targeting only that area where they're going to do Gamma Knife, for example, trigeminal nerve. We take high-resolution pictures to that area, and then they use those pictures for planning purposes for Gamma Knife. So, once the Gamma Knife is done, patient, they come back for a follow-up. Sometimes, it's a six-month follow-up. I normally ask them, "So, how did you feel Gamma Knife work?" and, if it works, and, for most of the times, it does work, they will be really happy, saying that, "Oh, actually, I can go out." Like, for trigeminal neuralgia, as you know, that it's very sensitive, they cannot go in the cold. They cannot shave that side of the face. And, if it's working, they'll be really happy, say, "Oh, I'm getting back to normal." It is actually very rewarding to be the part of the team who is actually helping patients, and you can see patients crying, and they're thanking us, and I'm always saying, "It's not me. It's neurosurgeons," but they will always say, "No, no. You're also part of the team," so it is actually really rewarding when you see that, after all your hard work, patients are being benefited. [music fades out]

**Heather** 32:41

So Dr. Hodaie, why is it so challenging to study pain in the brain?

**Dr. Hodaie** 32:46

Well, part of the challenge is because we have uniformly studied pain as a subjective experience. There are not any tests available. There's not any imaging available that actually allows us to see pain or to diagnose pain. We go by symptoms, and we correlate with what we find. So, for instance, by that, I mean if someone comes with terrible pain in the leg, for instance, we do an x-ray, we see a fracture, then we say, "Oh, sure. You have pain because of the fracture," but we're not able to see pain. So, we just correlate symptoms with whatever imaging we might have. For patients with trigeminal neuralgia, they have imaging, CT scans, MRIs, etc. They're generally reported as normal because they are normal. There's no tumour there. There's no vascular malformation. There's no, you know, unusual system, although, in some instances, in a minority of cases which we refer to, not as classical trigeminal neuralgia, but secondary trigeminal neuralgia. So in the vast majority of patients, the MRI looks normal. So then, what do we chase? I started studying different ways in which we can analyze brain imaging and the use of advanced forms of brain imaging so that we could gain, not just the view of what the brain looks like, but an understanding of what the microstructure of the brain looks like. What happens to the nerve? What happens to the brain in these conditions? And, one of the reasons why I think this is important is that, as much as the focus has been on this blood vessel, the blood

vessel, in a sense, is a bystander. The blood vessel does not feel pain. It's the nerve that feels pain, but we have not focused on the nerve so much because we could not really visualize the details of the nerve to the level that we wanted, and, you know, correlate that with symptoms, and so on. Whereas, with these forms of advanced brain imaging, we actually can. We focus more on the nerve. What happens in different segments of the nerve, what happens in the brain, how that correlates with pain, how that correlates with recovery from pain, and what are the different parts of the brain that are affected when a patient has experience with chronic pain, and so on?

**Heather** 36:16

And so, what are you finding?

**Dr. Hodaie** 36:17

Well, we found fascinating stuff. We have found that, in fact, the nerve is not quite normal in patients that have trigeminal neuralgia. There's parts of the nerve that are different in trigeminal neuralgia patients. We presume that this abnormality that we detect in patients with classical trigeminal neuralgia is the result of the ongoing compression of the nerve, and that, likely, this results in some thinning of its wall, which makes this aberrant signal transmission possible. But, the changes are not restricted to that spot alone. [gentle electronic music] As the nerve enters the brain, and then, from there, goes on to different brain areas, and so on, in fact, we're able to detect specific changes, and slowly, slowly, a picture has emerged that, if these micro-structural abnormalities are at the root of the nerve, then the patients are much more likely to respond positively to surgery.

**Heather** 37:19

Mm. So now, you have a way of figuring out the best treatment option for these patients, which you didn't have before?

**Dr. Hodaie** 37:25

Exactly. And then, when these abnormalities become more centralized, so then, we detect the abnormalities in areas of either the brainstem or beyond, then, likely, the patients are not going to be good responders. So, we are at the verge of, I think, a major clinical breakthrough, in that, I hope that very soon, we will be able to not only see patients and speak with them in clinic, and giving them an understanding of what their condition means, and what their treatment options are, but also, in the ability of having personalized representation of what the likelihood of benefit is for them, through the study of their clinical symptoms, as well as the details of their brain MRI. So you might think, "Well, you know what? Just ask them, do they have the pain, or don't they have the pain? And is that not enough?" Well, it's not that easy. But I'll tell you. If I were a patient, that would not be enough for me. And let me explain to you why. If I have a patient that comes to me with a structural problem – let's say they have a brain tumour – I would speak with them. I would show them the MRI. We would have a discussion as to how likely it is that this tumour can be fully removed, for instance. It's a visual representation that allows me also to think of what I can do, technically. So, if I have that conversation with my surgeon, I have a good idea -- a pretty good idea, when I go into surgery, of what this is going to be like. I am not, at this point, in 2022, able to offer this to my patients. When they come and see me, I'll tell them, "Yes, your symptoms are that of classical trigeminal neuralgia. I'm able to operate on you," while the immediate question would be, "Well, how likely is it that I will be better?" I cannot give them



anything that is individual for them. I would just tell them, "The vast majority of patients, 90% of them, will be better after surgery. What does it mean for you? I cannot say." I don't have any tools for that one person. So that means that the patient that has been suffering 10, 15, 20 years comes to see somebody and then, purely based on the trust that they placed in me, they agree to undergo general anesthesia, take on the risks of the things that I list off for them in the hopes that I will help them.

**Heather** 39:47

'Cause they are so desperate, based on the level of pain that they've been experiencing.

**Dr. Hodaie** 39:51

That's right. But, should we not want more for them, to really offer them better information when they make this decision, for them to know that the choice that they're making is informed? I truly am grateful for them for having so much faith in me, but surely, I really want to be able to offer them more than that, and for patients to make, again, choices that are relevant and applicable to them. This becomes also relevant when we think of, for instance, syndromes that we've uncovered, where the likelihood of success of conventional surgery is actually rather poor. So, about two years ago, we described a syndrome called single pontine lesion trigeminal neuralgia. It's a bit of a long name. But, these patients have a unique lesion deep in the brain that is rather unusual. We don't know exactly what it means. But, using our technique of advanced brain imaging, we've been able to pinpoint that it sits right on the fibres of the trigeminal nerve, deep in the brainstem, and it's not in keeping with something like multiple sclerosis. We know that patients with multiple sclerosis have a higher risk of trigeminal neuralgia, and the origin of that pain is a little bit different, not the blood vessel that I spoke of earlier on. But, the patients that have this unique syndrome have a likelihood of responding positively, or long-term response, which account as longer than one year being pain-free. The conventional procedures, only 5% of these patients will be long-term pain free.

**Heather** 41:25

And so, how many of them would make the decision to go down that route?

**Dr. Hodaie** 41:28

Well, that's the thing. The vast majority of these patients have been treated just as a straightforward, classical trigeminal neuralgia patient. So then, they have come to me after having had 5, 6, 7, 8 operations, and this is extraordinary. Whereas, if we take into account that these patients have a specific abnormality in the trigeminal fibres of the brainstem, and in fact, they respond better to neuromodulation techniques, then we bypass all the conventional treatments. We bypass all the potential risks that they could have. We don't allow patients to feel hopeless, having one surgery after another, and them not quite working out. And instead, we address the root of the problem, which is modulating the activity of these nerves as they bring information to the brain. So, that's why I think having a better paradigm, greater objectivity, and a proper, personalized approach to pain is truly the way forward. And, I hope that, through the work that we are doing, we really set the example and the right infrastructure for the whole of chronic pain to be approached this way. This is not unique to trigeminal neuralgia. In fact, I think trigeminal neuralgia makes an exceptionally good model for us to study how we can approach pain, and study it, so that then we can expand it to many other pain

syndromes, and truly have a way forward for this experience that has been magnificently difficult to work through.

**Heather 43:09**

Well, that's got to feel incredible, considering how many people experience chronic pain in this country and around the world and, you know, how little is available for them.

**Dr. Hodaie 43:18**

Absolutely. In fact, if you add up the number of people that suffer from chronic pain and, on the other hand, you add up the number of people that suffer from other disorders, such as heart disease, and so on, chronic pain is, by far, larger in numbers, and it really needs to be attended to, and we really need to advance the ways that we look after our patients. [uplifting electronic music]

**Josh 43:50**

I'm just so grateful to Dr. Hodaie because she gave me hope. There's no way to explain the level of hopelessness that you fall into with these things. I mean, she could change the world in any direction she wants to, and she's chosen to help out people like myself. I got a couple of good years, so far, and I don't know how long this will last, but if it ends tomorrow, I'm still going to have hope because I know that her team and her are still toiling away for the next big solution. So, hope is the most incredible thing to be given, especially when you have something that's kind of hopeless. [music fades out]

**Heather 44:37**

So, Dr. Hodaie, you've just heard from Josh how grateful he is for you, and for your work, and for your team. How rewarding is it for you, personally, to work in this field with trigeminal neuralgia patients, and also to be on the forefront of research? Why do you do it?

**Dr. Hodaie 44:51**

Heather, it's extremely rewarding. First of all, I'm so grateful that patients get better. I mean, that's plain and simple. I'm thrilled that that is the case. I think, particularly with this condition of trigeminal neuralgia, again, you know, it is an unusual condition that has been, in my view, not put at the forefront. So, I see this as really a labour that is – as challenging as it might be, sometimes – it's very much worth it. I will say also, that I get emails from all over the country, all over the world – emails from patients, emails from former trainees that have questions or want to run a specific case by me. I am honoured that they consider me in that light, to ask my advice. And, as wonderful as Josh's outcome is, which I'm, again, very grateful for, I know that there's a subset of patients that I have not been able to help. [gentle electronic music] And, I think it's our challenge to be able to help everyone to understand this condition better, to know what to do and to know what not to do, and ultimately set the stage for those that will come after me to have a better opportunity to help patients with facial pain, patients with other types of pain, and really move the field forwards. I think every labour that we do is not really the work of one person alone. It's a group and a team, and so, it's an infrastructure and a context. I don't want to have any, you know, major accolades for myself. My students are way smarter than I am. They spend their time studying, you know, different models of artificial intelligence, for instance, or different ways of processing, and post-processing brain images that, if I had to sit down and work through code and stuff by myself, well, I tell you, it would not take me five minutes like it takes these guys. But, they keep me

on my toes. They teach me all the time. And again, it's the work of a team, and I'm just thrilled to be part of this team. For as long as I remember, I have liked two things in life in terms of career: medicine and chemistry. And, I almost became an organic chemist, were it not for the fact that I was missing one math credit. [Heather laughs] [music fades out] Well, this is how life is. I did not become an organic chemist, and I have absolutely no regrets. I love what I do, and it keeps my mind engaged, 24 hours a day. And, what else can I ask for?

**Heather 47:39**

Well, we're glad you didn't become an organic chemist. We wouldn't be having this conversation today. [Dr. Hodaie chuckles] I don't want to let you go before talking about some of your latest research, because it's fascinating, specifically a paper that has recently come out about some innovative MRI techniques, right? Can you tell me about that?

**Dr. Hodaie 47:56**

Yeah, so our work in the research of trigeminal neuralgia has really focused on advancing how we image the brain and how we study the trigeminal fibres and the interaction of different networks in the brain that relate to pain. As of a few years ago, we realized that the conventional statistics that we have to assess all these areas, and MR voxels, and clinical datasets, and so on, was just not sufficient, so we moved into areas of artificial intelligence and machine learning, and this has proved to be quite important for us. We took nearly 1,000 MR images of normal patients that are available internationally, and so on, and we created an algorithm such that we could predict the chronological age of a person, based on their brain MRI so that, if the person is 25 years old, then, looking at their MRI, we can predict that they're 25. If they're 45, same thing. If they're 65, same thing. So, this allows us a very tight correlation between what we call brain age and their chronological age. So then, on top of this algorithm, or this model, we mapped patients that have trigeminal neuralgia and also some other pain conditions, and what we observed is that patients with trigeminal neuralgia are quite a lot older in the representation of their age on their brain than their chronological age by 10 years and more.

**Heather 49:54**

Okay, so what does that mean?

**Dr. Hodaie 49:56**

Yeah, suggesting that, in fact, chronic pain accelerates brain aging.

**Heather 50:01**

Mm.

**Dr. Hodaie 50:01**

And, importantly, this effect is driven primarily by women. Now, it turns out that trigeminal neuralgia is more frequently seen in women, and women also come to care and diagnosis later than men. So, this was fascinating for us to directly observe or did directly demonstrate, at least, that trigeminal neuralgia is associated with accelerated brain aging. And, we have now embarked on a number of other studies to understand what does it actually mean. Does our brain actually get older? Does our body get older? And, is this effect reversible or not? So, it's really sparked a huge area of interest that we're trying to

understand. Another aspect of this work, and this relates to two papers that we've recently published, is that patients with trigeminal neuralgia, also with other forms of chronic pain, but definitely with trigeminal neuralgia, come and sit down and talk to us, and it's quite common for them to say, "You know, with this pain, it's hard for me to function. I almost can't think clearly. I forget things. People have to remind me of things. I'm in conversations and, half the time, I don't remember what we talked about."

**Heather** 51:21

Sort of like a brain fog?

**Dr. Hodaie** 51:23

You can call it a brain fog. You can call it, you know, difficulty with focus and concentration. You know, it's different names that we can provide this, and oftentimes, physicians link this to patients being on medication, maybe some medication doing this to you, so on and so forth. Well, we studied the details of the hippocampus, which is the part of the brain that is involved in consolidation of memory, and, in fact, the hippocampus of patients with trigeminal neuralgia is significantly changed in volume. And, this is potentially one of the reasons, or at least linked or associated with the fact that patients have this ubiquitous complaint of having difficulties with memory, focus, and concentration. But, the good news is that, when patients with trigeminal neuralgia are relieved of their pain, the hippocampus normalizes in its structure. So, again, this effect is also driven primarily by women, and it speaks also to the dynamic structure of the human brain, and how it alters in the setting of chronic pain, and how, potentially, good intervention and early intervention can result in a normalization of those changes and, really, humans being able to gain their life back. So, when people recover from pain and say, "You know, I was absent for those years, and now I'm me again," I think we now are able to explain how this subjective sensation is actually represented in their brain. [electronic music plays]

**Heather** 53:08

Very exciting. Dr. Hodaie, thank you so much for joining us today and for telling us more about your research.

**Dr. Hodaie** 53:14

Thank you for giving me this platform and to have the opportunity also to really speak for many, many patients who are suffering as a silent disease. We just don't see their pain. [Your Complex Brain theme music plays]

**Heather** 53:30

Thank you to Dr. Mojgan Hodaie, Asma Naheed, and to Josh Johnston for joining us on the podcast today. [theme music continues] If you'd like to hear more about Josh's incredible story, and what life is like now for Josh and his family, head to our website at [uhn.ca/krembil](http://uhn.ca/krembil). This episode of Your Complex Brain was produced by Jessica Schmidt. Executive Producers are Carley McPherson and Tobin Dalrymple, with production assistance from Dr. Amy Ma, Twayne Pereira, Sara Yuan, and Suzanne Wice. If you enjoyed what you heard, please tell your family and friends, and leave us a rating and review on your favourite podcast listening app. Thanks for listening. We'll be back in two weeks with another exciting episode. Have a great day. [theme music fades out]