

## Season 1 – Episode 2 – Dr. Karen Davis

### 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 Christian Cote and today's guest on the podcast is Dr. Karen Davis, head of the division of Brain Imaging and Behavior, an award-winning senior scientist at UHN's Krembil Brain Institute. Dr. Davis is a pioneer in the research of pain. She joins us in a minute.

But first here's the backstory on Dr. Karen Davis. Growing up in Toronto Karen's earliest memory of a connection to science was watching the Jerry Lewis telethon for muscular dystrophy. She enjoyed the entertainers, but it was the scientists who came on the show to talk about their research and how it could impact patients, that intrigued her. Karen thought I want to do the same. And then in high school came an epiphany. A biology teacher told her class about a discovery. That the body releases endorphins to activate opiate receptors in the nervous system to help manage pain. That was Karen's light bulb moment and ever since she's dedicated herself to study the brain and how it processes pain.

Today her pioneering research has advanced our understanding of pain and how best to treat it. Dr. Karen Davis senior scientist at UHN's Krembil Brain Institute. Welcome to Behind the Breakthrough.

#### **DR. KAREN DAVIS**

Thanks very much. Happy to be here.

#### **BTB**

Fair to say pain is ubiquitous and yet is it also fair to say that it's not that well understood even in the world of health care?

#### **DR. KAREN DAVIS**

Absolutely. Everybody knows what pain is has experienced pain but we don't have a good understanding of what creates pain and and how to alleviate it.

#### **BTB**

So what is pain?

#### **DR. KAREN DAVIS**

Right, so that's the million-dollar question of course.

#### **BTB**

I'm glad I asked it.

#### **DR. KAREN DAVIS**

OK so pain you know we all kind of know what pain is. You know I don't think I've spoken with anybody that has not ever experienced pain. So, we know what ouch is. Kids know what pain is. They might not have the word for it yet when they're very young, but they certainly know the concept. So, when we think about a hurt or something that makes you go ouch that's inherently pain.

Giving a definition to pain is been a lot more challenging for those of us who study pain because the words that we use to describe pain or define pain can be restrictive. And so this has been a challenge that those of us in the field have continue to struggle with.

**BTB**

OK so let's dive a little deeper what's happening in our brain when we experience pain.

**DR. KAREN DAVIS**

Well first of all it's important to recognize that the term pain even though we struggle with what the exact definition should be.

One thing we all agree on who work in this field is that pain is a subjective experience. You know we might want to put other qualifiers on it in terms of it being emotional or unpleasant or aversive and that it in many instances leads to reactions to pain and motivates you to do something about the pain. But at its core when we say Ouch that's an experience. So, it's personal and it's subjective. When we start talking about how do you feel pain and why do you feel pain, now you're moving in to trying to link up what are the mechanisms in the brain and the spinal cord in your nerves that get triggered and create that perception.

**BTB**

When we say put our hand on the hot stove what's happening?

**DR. KAREN DAVIS**

That's kind of the classic kind of acute pain scenario which you know leads to the ouch and ultimately the reaction of you hopefully removing your hand away from the hot stove and learning not to perhaps do that again.

**BTB**

And that's part of why we feel pain.

**DR. KAREN DAVIS**

Exactly. So, in an acute situation pain is actually a good thing. It has protective functions and it helps you to remove yourself from a situation where you might have some very serious injury and also helps you to start to learn how to avoid those kinds of situations in the future.

So there's a lot of complexities to what happens when you touch that hot stove all the way from the receptors in your hand for instance that become activated and then relaying that information all the way from your hand into the spinal cord and up to the

brain and really the complexity of areas of the brain that start to respond is really quite amazing because the brain is really creating that very complex experience not just an ouch but that you know it's hot or burning where you're feeling the pain you know it's on your hand. So, your brain is helping you to figure out where it's located, it's triggering all sorts of mechanisms to have you remove your hand. So, motor responses it's triggering emotional areas in the brain to respond. And it's also leading to activation of areas of the brain that hopefully help dampen that pain.

**BTB**

Are there numbers that quantify how pervasive pain is in Canada?

**DR. KAREN DAVIS**

Absolutely. And it's really quite staggering the numbers that we've now recognized to represent the number of people who are experiencing chronic pain or living with chronic pain. And most estimates put that number around one in five in Canada, one in five in the U.S. and that also pertains to not just adults but also children living with chronic pain. So, in some situations in some types of pain those numbers are even higher. But generally, it's about 20 percent of the population. And when we first started to recognize that the numbers could be as high as 20 or even 30 percent. You know we all kind of paused and thought, seriously really? But all you have to do is really think about your own situation your inner circle of family and friends and then coworkers and you'll quickly realize that that number is actually quite correct.

**BTB**

And what's quality of life like for chronic pain sufferers?

**DR. KAREN DAVIS**

That's really one of the most serious issues for people who are living with chronic pain. It's not just that aversive emotional unpleasant sensory experience but it can take over their life and they have to make enormous adjustments. In many cases it can lead to difficulty or inability to to work or adjustments in their life. It obviously affects their relationships with their loved ones with their family with their co-workers. So, everything really is impacted because of what they're experiencing and what's the challenge for health care practitioners when it comes to managing that pain.

The challenge is multifold. You obviously number one are hoping to reduce that experience of pain and the intensity of it but more and more people are recognizing and people who are living with chronic pain are educating us who are the researchers that it's not just the intensity of pain it's the impact of that pain on all aspects of their life. So, for instance the ability to sleep. The ability to work the ability to go out and enjoy life or even do the most basic things shop interact with people care for your children. So, the challenge is not just to try to reduce the intensity of pain but to reduce how the pain impacts everything in their life.

**BTB**

Let's dive into your research then Karen what have you discovered when it comes to how we each react to pain?

**DR. KAREN DAVIS**

We've discovered and others have discovered that the variability from individual to individual and how they experience pain even in an acute pain situation is vastly different. And if you really just think about your own circle of friends and family you probably have a sense of how there are people who are quite stoic people who manage not just pain but many hardships in their life and others who seem to be more sensitive or have more difficulty in coping. So, there are real physiologic and brain differences amongst us all that contributes to this variability and you know frankly that's really the first step in recognizing that not all pain treatments are going to help for everybody that if we're experiencing pain differently either an intensity or in quality or in terms of how we cope. Then clearly there's a brain mechanism underlying that and that needs to be tapped into so that we can treat different people more effectively.

**BTB**

What have you found in terms of how the brain mechanism works in each of us individually?

**DR. KAREN DAVIS**

What we have found over and over again in both doing kind of behavioral tests to assess how much pain people are feeling but also looking in the brain to see how their brain is organized both in terms of structure and function. We see that there are links between how people experience pain and how the brain is functioning and how it's organized and really is quite a lot of variability. There are some differences for instance between men and women but there are just as many differences even within men or within women in terms of very very different brain organization and sense linked to how they experience pain.

**BTB**

From what I understand of what you've discovered some of us when we experience pain it's all consuming we feel it and we can't focus on anything else while for others they can focus their mind on something like a task or even meditate to help them endure or divert their attention away from the pain?

**DR. KAREN DAVIS**

That's right. Yes. So, what we kind of stumbled across about 10-15 years ago is kind of a system that we've called the AP system which stands for attention or pain. And what we kind of stumbled across is that when somebody is asked to do a particular task on a computer for instance and we're measuring how fast they do that task and how many errors they might make its kind of like a computer game. People are pretty similar in their performance but if every now and then we apply a painful stimulus to their hand while they're trying to do the task we assumed everybody would kind of stop or or slow down or make errors and that the pain would have quite of an interruptive impact on

their ability to perform this attention task. What we found is there was a huge variability and but half the people that we tested actually did the task better faster more accurate.

**BTB**

But that doesn't make sense, does it?

**DR. KAREN DAVIS**

Well we were astonished. We thought we must have measured something wrong and we start to just talk to people and the feedback we were getting from some of these people that we eventually called a types or attention dominates is that they were really more motivated and more focused when we delivered the painful stimulus because they really wanted to do well on the task and they wanted to maintain their performance or even do better. So, they really were able to kind of put the pain aside and shut it out and focus. We followed up that original study many times with other sorts of tasks and we keep seeing this difference amongst people in their ability to either kind of do a task in the face of pain or just even if they're not doing a task just kind of mind wander away from pain and then we started to do brain imaging of these very same people once we understood you know what their behavior was like whether pain was kind of disruptive or made them focus. And we found that a lot of the brain circuitry and brain anatomy was different for the people who could get pain out of their mind versus those that pain was like a disrupter. So, we've been finding that there's a lot of systems in the brain that help you modulate pain that is a little bit more flexible and able to kind of multitask with other systems in the brains of people who are these a types.

**BTB**

These mind wanderers who are able to cope with pain and in fact somehow perform a task better, do you know yet what's going on in their brains that allows them to do that?

**DR. KAREN DAVIS**

We're starting to think that it is this ability of some of the brain modulation systems and the systems that lead to pain perception to be more flexible and variable. So, it's kind of like they're less hard wired than in the brains of people who can't do that multitasking so they're able to kind of switch from one brain system to another more readily. And when people have chronic pain it could be that people who are not responding to chronic pain treatment might have this more of a fixed hardwired brain that isn't able to kind of switch around compared to some of these other people who might respond to a treatment.

**BTB**

I see, and this reaction in terms of the mind wanders, this is something that their brains are doing without any guidance from themselves, cognitively.

**DR. KAREN DAVIS**

That's right. They're just they're just kind of set up that way and we all know people who are you know able to multitask a lot and other people who might be better at focusing just on one thing at a time. So, it's like you know better or worse it's just a different way that their brains are kind of wired up in your research.

**BTB**

Are there other factors you've discovered that would influence how we feel pain how we experience pain.

**DR. KAREN DAVIS**

Well there's a lot of inherent personality factors that tend to exhibit when they're kind of in one group or another so a lot of things kind of go hand-in-hand. But what we're finding is that even some of those attributes which we kind of thought might be what we called you know a trait we've seen in some instances characteristics that we think or traits might actually be malleable so they might actually not be a trait but maybe just a state so a certain condition kind of like there are situations where people can have a situational state of depression not necessarily a chronic or clinical depression in the same way people might have certain states of some of these attributes that we might be able to tap into to modulate in the future.

**BTB**

And if you could just explain how a typical research project or test might work?

**DR. KAREN DAVIS**

In a kind of our quest to develop this personalized pain management approach. What we're hoping to do is get predictors of how people respond to certain treatments. The best way to do that is to first assess somebody before they have the treatment look at a whole host of things that we can look at in terms of their response to pain their ability to do these cognitive or attention tasks their ability to cope with multiple types of stimuli as well as I spoke before this kind of AP or mind wandering situation. And so, what we do is quite a comprehensive battery of tests to measure people's sensitivity to pain so to speak and also how well they can modulate pain in the face of these other concurrent situations. And we do brain imaging, so we know kind of the structure and function and how areas of the brain are connected to each other. How dynamic and flexible that connection is. And then we let them go through their treatment and we find out after their treatment if they responded well or didn't respond well and then we redo all the tests. So, using that kind of longitudinal approach we can do two things we can first of all look at how that pain management treatment whether it's surgery or drugs or stimulation of the brain or spinal cord. We can look at how that changed their brain and how it changed their behavior. But we can also separate patients into kind of responders and non-responders so we can look at the patients who got better after the treatments of their pain went down versus those that didn't seem to get any benefit from the treatment. So, now we have two groups the responders non responders and we go back and look at the data that we collected before they had the treatment and try to see if there was anything in that data that was predictive of whether or not they got better or not. So, this is kind of the approach that a lot of us in the field are taking to try to come up with predictive factors. Once we have enough of that data and we're starting to actually get some very good predictive factors then we'd be able to use those tests that were predictive to then feed back to the patient before they have the treatment and say you know you have a brain and responses to stimuli that we know sometimes predicts if

you're going to do well or not do well. And that's an extra piece of information they can use to decide whether or not to go ahead and have the treatment or not.

**BTB**

What I'm curious about is the times when you're introducing a stimuli to the patient what are we talking about? A pain stimulus.

**DR. KAREN DAVIS**

Sure yeah. So, we measure people's response to a variety of different types of pain stimuli some of them are thermal. Some of them are mechanical you know just touching the skin with a probe.

**BTB**

What's it like recruiting patients to saying you're gonna feel some pain in this test?

**DR. KAREN DAVIS**

It's easier than you think. Actually the patients who are going to have treatment are typically very very interested in participating in the research studies because they know that even though it might not impact their own personal treatment that it can contribute to better treatment approaches in the future. So, they're usually very willing to participate and we always have to kind of match any study in patients with kind of healthy controls to see how that differs and we also have a lot of people who are quite willing to volunteer to do our studies. It does contribute to science and they feel good about that.

**BTB**

So in terms of translation from research to patient how might your research inform doctors when it comes to managing their patients pain?

**DR. KAREN DAVIS**

What a lot of us in the field are trying to do is work towards what we call personalized pain management so personalized medicine we see in all aspects of medicine these days for cancer treatment it's personalized based on a person's particular tumor all sorts of areas of medicine. In terms of pain management, the idea is that we need to understand how different treatments are effective for different people and why. So, I'll give you one example. There is one type of drug that is used for some people who have chronic pain and that drug, we understand what neurotransmitters it affects in the spinal cord in the brain. It turns out that we also know that neurotransmitter system is reflected by people having a certain type of sensitivity to pain stimuli that we can test using a very quick test. It takes about 10 seconds. So, one indication of whether or not that drug may or may not work in that person is to just do this very quick behavioral test and that might give us insight into knowing whether or not that neurotransmitter system is kind of ramped up in that person or has the capacity to be suppressed. There's another behavioral test that we've been studying, and many people have also been studying that is also linked to a system in the brain that modulates pain. And again, different people have a different capacity to modulate or dampen their own pain. So, what we're trying to

do is make that link between the brain and this behavioral tests. And again, this behavioral test we might be able to do in you know 20 minutes without putting somebody in a scanner. And that would give again the physician some additional information that that that particular drug may or may not work in that person.

**BTB**

So, down the road could we see a world where we could test a patient and determine their pain profile whether they're a pain focus or a mind wander to help doctors design this more personalized pain management regimen?

**DR. KAREN DAVIS**

That's exactly what we're trying to do both in our lab and around the world so we're trying to come up with these kind of biomarkers that will predict whether or marker but well a marker any sort of marker could be the result of a behavioral test. You know how sensitive you might be to pain or how you react to certain type of stimuli. It might be a blood test. It might be measuring certain cells in your body. It might be testing for certain genetic markers. So, there's a whole host of tests that people are developing that we're trying to link to responses in the brain and how people are feeling pain. And so down the road what we're hoping is that you can undergo a whole bunch of tests that hopefully isn't too invasive and that might give you a profile that matches a certain type of therapy. Now that might not be a drug it might be some other sorts of approaches to manage pain might be behavioral cognitive behavioral therapy. It might be a neurosurgical approach. It might be physical therapy could be a whole host of therapy meditation. It could be meditation. So, what we're trying to do is reduce how many treatments people are trying unsuccessfully which is exhausting for the patient. It very expensive to the health care system trying on the patient and very trying on the patient and time consuming. So, if we can have more targeted therapies this is this is better for the patient for their families and for the health care system.

**BTB**

You're listening to Behind The Breakthrough, podcast about groundbreaking medical research and the people behind it at the University Health Network in Toronto Canada's largest teaching and research hospital. I'm your host Christian Cote and we're speaking today with Dr. Karen Davis award winning senior scientist at your UHN's Krembil Brain Institute for her pioneering work in the research of pain.

Karen as I was preparing for our interview, I was fascinated to learn that we've been studying pain for centuries going back to scholars such as Descartes in the 1600s. And yet even as you said the complexity of pain and chronic pain today are still not well understood why is that?

**DR. KAREN DAVIS**

I think a couple of factors. One is the variability across people. So, we all do experience pain a little bit differently when we're exposed to the exact same stimulus. So, that's been I think a hardship in the past because people are used to doing research where



they develop an experiment and they measure something and they kind of pull all the data from every subject that they measure it from and they look for kind of a reason for that that pain experience. And there was always a lot of variability in that data. And I think we kind of missed the boat for decades or even hundreds of years by trying to look for one common mechanism and really until brain imaging came along we didn't really appreciate how different our brains were even though we know inherently that you know we all have very different experiences so that was one of the reasons and the other reason is that a lot of times when people were developing different types of experiments they were very focused until recently on trying to measure what we called the intensity component of pain until the last 10 15 years or so. Most pain studies simply asked people to rate their pain from zero to 10 or zero to 100 on an intensity scale. How much pain are you feeling? And we all know that pain is not just how much it's what is it you know it's the quality and that nuance was really not looked into very much in the past so. So, I think there were a lot of areas of the brain for instance that weren't fully appreciated in terms of their contribution because we weren't looking at the limbic system which might represent the emotional part of pain and this sort of thing. So, we're getting much better at that now with a much more holistic approach.

**BTB**

Given the stakes that we talked about at the beginning in terms of the number of Canadians suffering one in five especially in terms of chronic pain what kind of pressure do you feel every day going into work to translate your research to something that doctors can use to apply to patients.

**DR. KAREN DAVIS**

So that's interesting question. I have never really looked at it as pressure *per se*. I see it as a motivator more than pressure. I think if you feel pressure you might almost give up. But I think most of us in the field the more we interact with patients or read about these statistics and hear more personal stories the more it motivates us to work hard try to think outside the box maybe come up with different approaches because there are people that are really in need.

**BTB**

And yet science takes time you know how do you reconcile that urgency to come up with a more elegant solution to pain for people when we know the rigor of science demands step by step?

**DR. KAREN DAVIS**

That is a fine balance because there's always the pressure to put something out there but we do have very rigorous approaches. There are systems to ensure that we don't roll out something that's kind of not ready for prime time.

**BTB**

I imagine in your work you experience setbacks or failure, how do you deal with those challenges?

**DR. KAREN DAVIS**

That's a good question. I think anybody any academic has to develop a way of coping with failure and I'd like to use kind of a baseball analogy you know a really good hitter in baseball has a batting average of maybe three hundred which means they fail 70 percent of the time and yet they're a superstar if they have a batting average of 300. So, we kind of have to think of ourselves as being scientific baseball players that failing 70 percent of the time is OK if we succeed 30 percent of the time, we're doing pretty good. So, we have to kind of learn to take criticism and get back up on the horse and keep going again.

**BTB**

Do you ever have doubts?

**DR. KAREN DAVIS**

We all have doubts, but I think what drives most of us is just a very fundamental curiosity in trying to understand. I think if we set our goal on something like a cure or you know the magic bullet that's going to help everybody. You're kind of setting yourself up for failure because that's not how discovery happens you have to just keep in mind that this science can be fun and it's can be really exciting and every now and then you get an aha moment doesn't happen that often but if it happens a couple of times in your career that's outstanding. That's the home run.

**BTB**

I'm curious along the way in terms of your career trajectory, how much you benefited from mentors along the way? Like what is it they gave you that benefited you?

**DR. KAREN DAVIS**

Oh, I've had fantastic mentors along the way. The benefit it's kind of gives you a picture of what success looks like. It also gives you a picture of what it looks like to plow through difficult times or failure. So, I think my mentors have always been very positive people that never let a failure kind of get them down and just tried to learn from something that didn't work and go off in a different direction and really have joy in the science. So, I think that's what they've shown me and also a lot of my mentors really enjoyed being mentors and interacting with students. And so I gained a lot from them in that way. And what's your approach to mentoring people today. I try to emulate some of my mentors in that I was always given a lot of guidance but a tremendous amount of flexibility to develop my own ideas and I didn't realize how unique that was. Most of the labs that I trained in allowed me to come up with an idea and to kind of run with it. And most labs don't really let their students do that. So, I've tried to have the same kind of approach in my lab that my students will usually say Oh the first time you approach it with a new idea. You know she'll probably say no that's never going to work but you know, they push me a few times. I usually reconsider. It's like OK let's run with that. And most of the really exciting stuff that has come out of my lab over 25 years have really come from a seed of an idea from a trainee. Absolutely.

**BTB**

It can also be instructive for those just starting their career to hear from successful people about their career path, what did it take for you to get where you are today?

**DR. KAREN DAVIS**

A lot of perseverance as they a lot of patients and I think when I was training, I think there was less pressure to find your path early on. So, I did several post-doctoral fellowships and I tried different things. I also you know I retooled as I said I started off studying single cells using electrophysiology. I moved from animal models to human models and then I moved to brain imaging when that was invented. So, I was kind of willing to retool and to try a different approach. And so, I try to tell trainees that they should be open minded to what might come in the future. You know MRI eyes weren't invented when I was an undergrad student let alone functional MRI so. So, sometimes you never know where the technology is going to go. And I think it's maybe wiser to find your passion in terms of the subject that you're interested in and then learn the technique that you need to learn to understand that topic.

**BTB**

How did you know when you had hit your passion?

**DR. KAREN DAVIS**

As you mentioned in your opening. I kind of had this passion for trying to understand the brain and how we modulate pain back in high school. That's quite unusual. I think probably to have an area that grabbed your attention so early on, but it was just being at the right place at the right time.

**BTB**

What's your advice then to young aspiring scientists out there but not sure of what to do next?

**DR. KAREN DAVIS**

The best advice I could give is to again find your passion and also decide if an academic life is really for you. There are many ways you can make a contribution to science it doesn't have to be through an academic path and an academic path is difficult. It's not necessarily going to be open to you if you're the best thinker with the highest marks and the best accomplishments. It's a little bit of luck finding opportunities to get a position in a university when one happens to be available so it's a bit of a timing issue that doesn't always work out for everybody. So, I would say relax a bit. Be willing to be a starving student for a little bit longer and also think about what it is you really want to do with your life.

**BTB**

What drives you? Why do you do what you do?

**DR. KAREN DAVIS**

It is fun. We sometimes lose track of that but trying to understand how the brain works is kind of the best job in the world. Having the freedom to ask questions and to pursue

those questions is the best job in the world. And if at the end of the day the information that you accumulate and discover may actually help people who are suffering from pain you know that's the best job in the world.

**BTB**

At the outset we mentioned how you when you first got into this field your desire was to have impact, how would you rate your performance in terms of achieving impact to date?

**DR. KAREN DAVIS**

I might have started off with that desire to have impact. What took over was the curiosity and just the interest in understanding and then as you age you kind of slowly come back to that, what will be my impact once I'm done with my career? So, I think I have had impact in not just the actual discoveries that have come out of my lab but hopefully in the trainees that I've either personally mentored or helped to mentor many of them are off doing great things now and that's going to continue to advance the field and I'm also trying to have impact in terms of society. One of the areas that I've been involved with and developing more of it is research and understanding of issues surrounding the privacy of brain data and the ethical issues on the neuro ethical issues surrounding what we do with the brain data that we're collecting and down the road hopefully working with policymakers to try to ensure that we can do this science and we can have treatments. But we need to have protection of that information.

**BTB**

So what can we look for next coming out of your lab?

**DR. KAREN DAVIS**

Well we have a lot of exciting projects underway now looking at again predictive kind of markers of treatment outcome for a variety of different types of chronic pain and different treatments. So, that's the main focus in the lab. And then the other focus as I just mentioned is to try to start to get a better understanding of what people are concerned about in terms of the use of brain data and protection of brain data. And so we're spending a considerable amount of time looking at these new right ethical issues.

**BTB**

Dr. Karen Davis award winning senior scientist at UHN's Krembil Brain Institute. Thanks for speaking with us and continued success.

**DR. KAREN DAVIS**

Thank you very much.

**BTB**

For more on the podcast go to our website [www.behindthebreakthrough.ca](http://www.behindthebreakthrough.ca) Let us know what you think, we love your feedback. That's a wrap for this episode of Behind The Breakthrough, the podcast all about groundbreaking medical research and the people

## Behind the Breakthrough Podcast – University Health Network

behind it at University Health Network in Toronto, Canada's largest teaching and research hospital. I'm your host Christian Coté. Thanks for listening.