

IS STRESS
CONTAGIOUS?



KEEP YOUR BRAIN
FIT & HEALTHY



MANAGING
CHRONIC PAIN

YOUR HEALTH

by UHN'S Krembil Brain Institute

THE SCIENCE OF STRESS



Your brain. Our purpose.

UHN's Krembil Brain Institute (KBI) is home to one of Canada's largest and most specialized teams of physicians and scientists working together to find new treatments for brain diseases and disorders. At KBI, we have **one goal** – to help the millions of Canadians living with brain-related illnesses live longer, healthier lives.

EPILEPSY

Many women with neurological disorders go undiagnosed, but that's changing.

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MEMORY

You can improve your memory by using simple, repetitive techniques.

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CONCUSSION

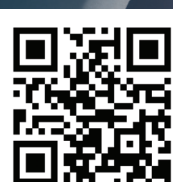
KBI researchers are searching for biomarkers to help diagnose concussion earlier.

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CHRONIC PAIN

Releasing your body's 'inner pharmacy' can help reduce the effects of chronic pain.

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ALZHEIMER'S

A new theory that Alzheimer's may be an autoimmune disease could open up a whole new area of research.

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STRESS

Researchers have discovered that stress is contagious – especially for women.

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PARKINSON'S

Deep brain stimulation has been life-changing for many patients.

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SCIENCE-BASED TIPS TO KEEP YOUR BRAIN FIT & HEALTHY

Eat healthy

Your brain is only two per cent of your body weight, but it consumes 20 per cent of your body's energy. With the right fuel, your brain releases its 'inner pharmacy' – neurotransmitters like dopamine and serotonin – key players in mood changes, digestion and sexual health. So choose a diet

that's colourful, low in processed food and refined sugars, and has a variety of nutrients and food groups.



DR. ANDREA FURLAN

Senior Scientist, KITE Research Institute
Physician, Toronto Rehabilitation Institute



Get some sleep

Research points to a strong relationship between good sleep health and the likelihood of maintaining good brain health later in life. Stick to a schedule so your body gets used to sleeping on a regular basis. And make sure your bedroom is restful – no watching the news or playing on your phone right before bed.



DR. MARY PAT McANDREWS

Senior Scientist, Krembil Brain Institute
Division Head, Clinical and Computational Neuroscience, Krembil Research Institute



Try new things

Your brain is complicated. It's built on many, many connections, and the best way to keep these connections thriving is to learn a new hobby, a new skill or do something that's going to keep your brain engaged, such as learning a new language or musical instrument. Make it challenging, make it complex, but make it something you enjoy.



DR. DONALD WEAVER

Neurologist, Krembil Chair in Drug Discovery Research for Alzheimer's Disease, Krembil Brain Institute



Be social

Social interaction is a basic biological need in the same way hunger is a physiological one. What's more, interacting with friends, family and even strangers can release the same chemicals in the brain that are associated with rewards, such as dopamine and oxytocin. These interactions may also reduce the long-term effects of stress.



DR. JAIDEEP BAINS

Director, Krembil Research Institute
Co-Director and Senior Scientist, Krembil Brain Institute



Keep moving

Regular physical activity and exercise can improve the blood flow to your brain, reduce inflammation, improve brain immune-cell health and protect it from illness. Start with 10 minutes and then build up from there, but make sure you do something every day. Take a friend with you, walk with the dog – everything counts.



DR. ALEKSANDRA PIKULA

Clinician Investigator, Krembil Brain Institute, Jay and Sari Sonshine Chair in Stroke Prevention and Cerebrovascular Brain Health



What if Alzheimer's isn't just a brain disease?

A Canadian scientist's eureka moment may lead to new approaches in Alzheimer's research and treatment.

LINDSAY BONGARD-BATORI still remembers the frustration and sadness she felt as the slow advance of Alzheimer's disease took away what should have been some of the best years of her mother's life. "My mom, Barbara, was my person – nothing explains it better than that," she says. "She loved going for long walks and just appreciating the little things in life."

As time passed, that began to change. "She started repeating herself a lot. Then she started forgetting things. I remember one day she called me, crying. She had gone to the grocery store and couldn't find her car even though the parking lot wasn't that big. She was hysterical, and I had to talk her through it. We decided as a family, with her involved, that it was time to talk to her doctor."

Those discussions eventually led to a diagnosis: Barbara was suffering from mild cognitive impairment, a common precursor to Alzheimer's disease. Not long after, she suffered a frightening fall, which led her daughter to find a place that could provide additional care. It was a painful time for Bongard-Batori and her family. "They say with Alzheimer's, you mourn twice, and I understood right then what that meant," she says.

Novel thinking, new theories

It's estimated that more than 1.7 million Canadians will be living with Alzheimer's disease by 2050, three times the current number, according to the Alzheimer Society of Canada. Factor in the one million or so care partners needed to support this unprecedented increase, and the sheer volume of Canadians whose lives may one day be upended by the disease is staggering. "These numbers are a wake-up call for our system – we can't keep going



DR. DONALD WEAVER has designed and co-developed two Alzheimer's drugs that have reached Phase III human trials and has four others in preclinical development.

the way we are," notes Dr. Donald Weaver, a Senior Scientist at UHN's Krembil Brain Institute and the Krembil Chair in Drug Discovery Research for Alzheimer's Disease.

To Dr. Weaver, that means thinking outside the box, even if it raises questions about everything we think we know about the disease. He's come up with a novel theory as to why Alzheimer's develops: it may be an autoimmune disease that attacks the brain. The idea challenges the prevailing view, which contends that the buildup of a peptide called beta amyloid in the brain is a key factor in the development of the disease.

"We're arguing that amyloid is, in fact, a normal part of your brain," Dr. Weaver explains. "It's part of the immune system in your brain. It's supposed to be there. The second notion our theory is based on is that, unfortunately, the immune system in your brain cannot differentiate between a neuron, which is a brain cell, and bacteria, which is an invading pathogen."

This means that when your brain's immune system is activated, be it by head trauma, excessive air pollution or an infection – at any point in one's life – the beta amyloid that is sent to help may actually attack the very neurons it is trying to protect. "As those brain cells are killed, they release their products as they fall apart," Dr. Weaver says. "That turns on more inflammation, and this becomes a vicious cycle that goes on for decades and decades."

"The brain is just so crucial," he adds. "It's so complicated, and that's why the idea of an autoimmune disease of the brain – which is what we are proposing – is so devastating."



↑ **LINDSAY BONGARD-BATORI** lost her beloved mother, Barbara, to Alzheimer's in 2020.

Future drug discoveries

The implications of this theory are enormous. If the factors that lead to Alzheimer's disease accumulate from an early age, potentially even from childhood, they need to be taken much more seriously, says Dr. Weaver, adding that finding this new theory was a "eureka moment" in his lab.

It's also "the most exciting time of my life," he says, "because this is an opportunity for us to make drugs that address a target that we've discovered ourselves and targets that we think are the fundamental, underlying cause of Alzheimer's disease."

That's exactly what Bongard-Batori and the many others living with the impacts of Alzheimer's and dementia want to hear. "It makes me angry that there isn't a cure yet," she says. "But I hope in my lifetime that I get to see some progression. We hope it's coming." **YH**

10

WARNING SIGNS OF DEMENTIA



1. Memory changes that affect day-to-day abilities
2. Difficulty doing familiar tasks
3. Changes in language and communication
4. Disorientation in time and place
5. Impaired judgment
6. Problems with abstract thinking
7. Misplacing things
8. Changes in mood, personality and behaviour
9. Loss of initiative
10. Challenges understanding visual and spatial information

SOURCE: ALZHEIMER SOCIETY OF CANADA

"Memories are stories we tell ourselves about ourselves."

There are ways we encode, retrieve and represent all the things that have happened in our lives. That allows us to revisit our past, to plan for the future and to solve real problems in the present."

—Dr. Mary Pat McAndrews

"Memory is a living thing. **The way you learn a memory is different from how you retrieve it,** so there are a lot of factors, like how you're feeling at the time you've had the memory, that impact how we later recall it."

—Dr. David Gold

"Our memory is like a scrapbook, but not one that perfectly preserves the events we experience."

Sometimes we can retrieve information that seems almost lost to us in terms of the fine details of how we first came to learn that information. Sometimes our memories are as vivid as opening a picture we saw last week because the brain's been able to store and retrieve all those finer details, while other times it's fuzzy or indistinct, but we still have the general gist. But there's really a gradient in terms of the information we can remember and how it's delivered back to us." **—MPM**

"Alzheimer's and temporal lobe epilepsy both impact the limbic system, the same real estate in the brain where the hippocampus lives, which is **an important area for generating episodic memories.**"

For those with damage to that region, memories can be impacted. It can be very frustrating, with people across both populations saying they have difficulty vividly recalling events and forming new memories." **—DG**

THE MYSTERY OF OUR MEMORY



Krembil's Drs. Mary Pat McAndrews and David Gold on the scrapbooks of our mind.

"We're part of a study that looks at individuals with mild Alzheimer's disease to see whether **deep brain stimulation,** the kind that is used in Parkinson's disease, can be used to get the memory circuits more active or available – juice them up a bit if they're too quiet – to make the hippocampus a little more lively." **—MPM**

"Another study looks at people at risk for developing Alzheimer's. There's a new hypothesis that early on in the disease **the hippocampus may be too active** and you need to get it a bit quieter. We're using a drug that's used in epilepsy to see whether quieting down that activity can be beneficial to memory in the short term and potentially prevent Alzheimer's from developing down the road." **—MPM**

"We're **teaching strategies to help people learn and retrieve information in more efficient ways.** For instance, if you're thinking, 'I have a family reunion coming up, and I can't remember which uncle goes with which kids,' then one strategy would be retrieval practice, where you practice pulling out long-term information from your own memory. The challenge is not just encoding the memory, but also pulling it out of your own memory storehouse. So if you're retrieving it on your own, you're giving yourself some retrieval practice, which could be beneficial for retaining that memory." **—DG**

CLOSING THE GAP

Why women with neurological disorders often experience a delay in diagnosis.

LIKE MANY PEOPLE, Nikki Ashworth thought she knew what epilepsy looked like. She pictured the severe full-body seizures, triggered by flashing light, that leave sufferers flat on the ground. Ashworth suspected the sensation she often experienced while crossing a street – an intense minute-long sense of déjà vu and overwhelming dread, accompanied by the physical feeling of heat rising from her stomach to her head and then dropping her down like a roller-coaster – was unusual, but the thought that it might be a symptom of epilepsy never crossed her mind.

As Ashworth’s episodes started to increase, occurring up to 10 times a day, her boyfriend suggested she visit a doctor. After Googling “medical déjà vu,” Ashworth discovered something called focal aware seizures, with a description that matched her symptoms almost to the letter. While she was confident in her self-diagnosis, the doctor she saw disagreed. “Oh, maybe you’re having panic attacks,” he said. Her response: “That is not what is happening.”

He finally referred her to a neurologist, who ordered an MRI. Ashworth was diagnosed with temporal lobe epilepsy on the right side of her brain. They also found a small benign tumour. “People would not notice I was having seizures at all. I’ve hidden them my entire life,” she says. “That’s why I wasn’t diagnosed until I was 37.”

Ashworth’s story is hardly an outlier when it comes to diagnosing neurological disorders in women. All too often, women are taught to ignore irregularities within their brains or are dismissed when they are diagnosed with headaches, brain fog, anxiety or depression – which are often, but not always, symptoms of a neurological disorder. It’s a topic Dr. Esther Bui, a neurologist and clinician educator at the Krembil Brain Institute, has made a centrepiece of her work. Dr. Bui specializes in exploring how a woman’s experience with a neurological disorder may differ from a man’s and why they have a higher likelihood of being misdiagnosed or underdiagnosed.

→ **NIKKI ASHWORTH** has lived with temporal lobe epilepsy her whole life, but wasn't diagnosed until her 30s.



“MY ADVICE TO OTHER WOMEN IS TO ADVOCATE FOR YOURSELF, BE PERSISTENT AND DON’T GIVE UP. KNOWLEDGE IS POWER.”

— NIKKI ASHWORTH

The big picture

Biology is certainly part of the issue, Dr. Bui notes. Hormonal fluctuations during puberty, pregnancy and menopause can alter the way neurological problems manifest during a woman’s life. For example, pregnancy complications such as gestational hypertension may trigger cognitive issues decades later. In addition to physical differences, women are more likely to have increased caregiving or other personal responsibilities that can delay a trip to the doctor or cause symptoms to be misdiagnosed as poor coping, depression or anxiety.

Looking at a woman’s whole being and taking a precision-medicine approach can help

specialists better recognize neurological symptoms. “In addition to recognizing that there are biological factors to the patient you’re caring for, there are psychosocial factors as well,” Dr. Bui explains. “Having that integrated approach of considering both sex and gender in neurological care provides the chance to give true precision-based medicine.”

More research needed

The lack of neurological research focused specifically on women may be having significant consequences on those who want to start a family, says Dr. Bui. She’s heard too many stories of women who have epilepsy being told it would be irresponsible to have children or that medication could almost certainly damage their unborn child. Women with epilepsy have felt selfish and stigmatized for wanting to have a family. “That’s counterintuitive to everything I know, having met hundreds of women who hope to remain seizure-free and are determined to have a healthy pregnancy,” she says.

Dr. Bui, as well as colleagues like Dr. Mary Angela O’Neal from Harvard University and the Brigham and Women’s Hospital in Boston, hope that continuing research will increase options for patients who want to start a family. “When we’re treating a woman who desires a pregnancy, we have to think about the huge benefit that is. And it often outweighs the risks. The absence of data doesn’t mean it’s not safe to do it.”

Both Drs. Bui and O’Neal say more research is needed to gain a better knowledge of women’s experiences, and that doctors should also examine their own biases when diagnosing women patients. That support may help people like Nikki Ashworth to recognize symptoms and receive diagnoses earlier in life.

“Nikki’s story is really a gift,” Dr. Bui says. “She’s advocating for other young women who may have been ignored and shedding light on the nuances of seizure symptoms so healthcare providers can better recognize when seizures sound like what she described.” **YH**



DR. ESTHER BUI
created Canada's first accredited Women's Neurology Clinic and training program.



DR. MARY ANGELA O'NEAL
directs a Harvard Medical School course in Women's Neurology and Psychiatry.



YOUR BRAIN ON STRESS

GIVE YOURSELF A BREAK

A few minutes of mindful breathing daily can clear your mind and relax your body, says Dr. Kathryn Curtis, a clinical psychologist at the Comprehensive Integrated Pain Program at University Health Network. Studies show that

mindfulness can benefit various neurological, cardiovascular and mental health conditions.

"Stress can impact pretty much every system and physiological process in the body," she says. "If we can carve out even a few minutes a day to combat stress through different mind-body

approaches, including mindfulness, then we can turn the tides of stress in our minds and our bodies."



SCAN THE QR CODE

to access a 5-minute mindfulness exercise Dr. Curtis recorded for readers.



DR. JAIDEEP BAINS

researches how the brain processes, activates and adapts to stress.



DR. KATHRYN CURTIS

studies the impact of mind-body interventions on individuals with disabilities or chronic pain.

We all know how stress feels, but how does it affect our brains?

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VERYONE CAN SPOT the telltale signs of stress – a racing heartbeat, sweaty palms, rapid breathing, anxiousness, irritability and rushed mistakes – but what happens in our brain and body when our stress response is activated?

That's what Dr. Jaideep Bains, Senior Scientist and Director of the Krembil Research Institute, is trying to find out. By understanding the effects of stress on the brain, he hopes to develop behavioural and pharmacological therapies to help mitigate its effects. Here's what he's learned so far.

The chemistry of stress

When you're stressed out, your body releases hormones, including cortisol, which helps control your body's metabolism and immune system. It also releases adrenaline, the hormone that triggers the fight-or-flight response. Internal struggles like writing an exam and external threats like sitting in an overcrowded room trigger different neural pathways and chemical responses, but the production of cortisol happens in both instances. This is important, says Dr. Bains. "It's not directly helping you respond to the threat in front of you, but it is helping you recover from stress." It also affects different regions in the brain to help you react more effectively the next time.

Importance of stress

Stress may feel uncomfortable, but it's an important trait that helps us respond to challenges and

maintain our internal homeostasis – our internal state. "That's why the stress response exists," explains Dr. Bains. "Without it, we wouldn't be able to deal with any kind of challenges in our environment." While too much stress is bad, studies show there's an optimal amount of stress that's useful to every organism. "This idea has emerged that you want this kind of Goldilocks zone of stress in your life," he says. "Little challenges that you need to overcome."

Is stress contagious?

Physiological conditions tend to impact individuals, but stress is an exception. It can trigger a response in others, says Dr. Bains. When we're stressed, we send out signals that alert those around us and even bring them toward us. "Others then gain information about what you may have experienced," he explains. "Another individual doesn't have to be exposed to a threat, but they benefit from your experience by learning about it." Research has shown that stress can be transmitted in people through cues in our sweat. Others can tell the difference between "stress sweat" and "normal sweat."

Treating stress

There may be no cure for stress, but researchers like Dr. Bains are exploring ways to treat disorders that are linked to stress, like depression and anxiety disorders. Neuromodulation, which involves stimulating areas of the brain from the outside using a focused ultrasound, is a promising approach.

The role social interactions can have in lowering the long-term impact of stress is another area of interest for researchers. There are also distinct gender differences, he notes. "The long-term consequences of stress on neural circuits can be erased by social interactions in females, but we don't see that in males," he says. "Still, if you can surround yourself with positive people, that's probably a great thing."

But the research Dr. Bains is most excited about? The potential to change different patterns in the brain. "The ability to modify neural circuits to set you up to better manage stress – that's where the real hope lies," he says. **YH**

Understanding chronic pain

Scientists at Krembil are finding new ways to treat a condition you can't see.

EVERYONE HAS FELT acute pain, but for more than eight million Canadians, chronic unrelenting pain is part of everyday life.

“It’s an invisible disability,” says Dr. Andrea Furlan, a senior scientist at the KITE Research Institute and a physiatrist with the Toronto Rehabilitation Institute at University Health Network (UHN), about what’s known as chronic pain. “I’ve had patients tell me they wish they had an amputation, cancer or a scar so people would take them seriously.”

“The International Association for the Study of Pain agrees that anything beyond three months should be considered chronic pain,” notes Dr. Anuj Bhatia, Director of the Comprehensive Integrated Pain Program at UHN and a clinician investigator with the Krembil Brain Institute.

Chronic pain often comes on after a surgery or injury, or is part of a condition. Most people experience pain during the first six weeks after an injury, with

those feelings subsiding within the next six weeks. Sometimes, though, the pain doesn’t disappear.

Dr. Furlan compares the body’s pain system to a home fire alarm. There may have been a reason to set off the alarm, but when it continues to blare, even after the smoke has cleared, something is clearly wrong with the system itself – that’s chronic pain. “Now you have to call the alarm company to fix the system,” she says. “Myself and Dr. Bhatia, we are the doctors of the alarm system.”

Searching for answers

Drs. Bhatia and Furlan are both actively researching the way the brain processes pain and how chronic pain differs from acute pain. Using functional magnetic resonance imaging (fMRI) – a live look at how blood flows through the brain – scientists have gained a better understanding of the change that takes place between acute and chronic pain.

With acute pain, the area of the brain associated with the body part that hurts lights up on an fMRI. When someone begins experiencing chronic pain, that



↑
LARA PINGUE, pictured here with her husband and two children, was a runner and practiced yoga when she suffered a herniated disc in her lower back in 2018. The injury took months to be diagnosed, and her acute pain gradually transformed into chronic pain.

Pingue tried everything from physiotherapy to medication to steroid injections to surgery, but nothing eliminated the pain entirely. “When the pain was at its worst, it was like a screeching, loud alarm bell going off,” she explains. “Now it’s like a hum, but the sound is always there. That’s how I describe living with chronic pain.”

same area lights up, but so do peripheral areas in the brain associated with emotions like anxiety and depression.

“Pain is not just a sensory, biological phenomenon that is coming from the tissue that is damaged or diseased,” notes Dr. Furlan. “It is a combination of many factors. But all pain is real.”

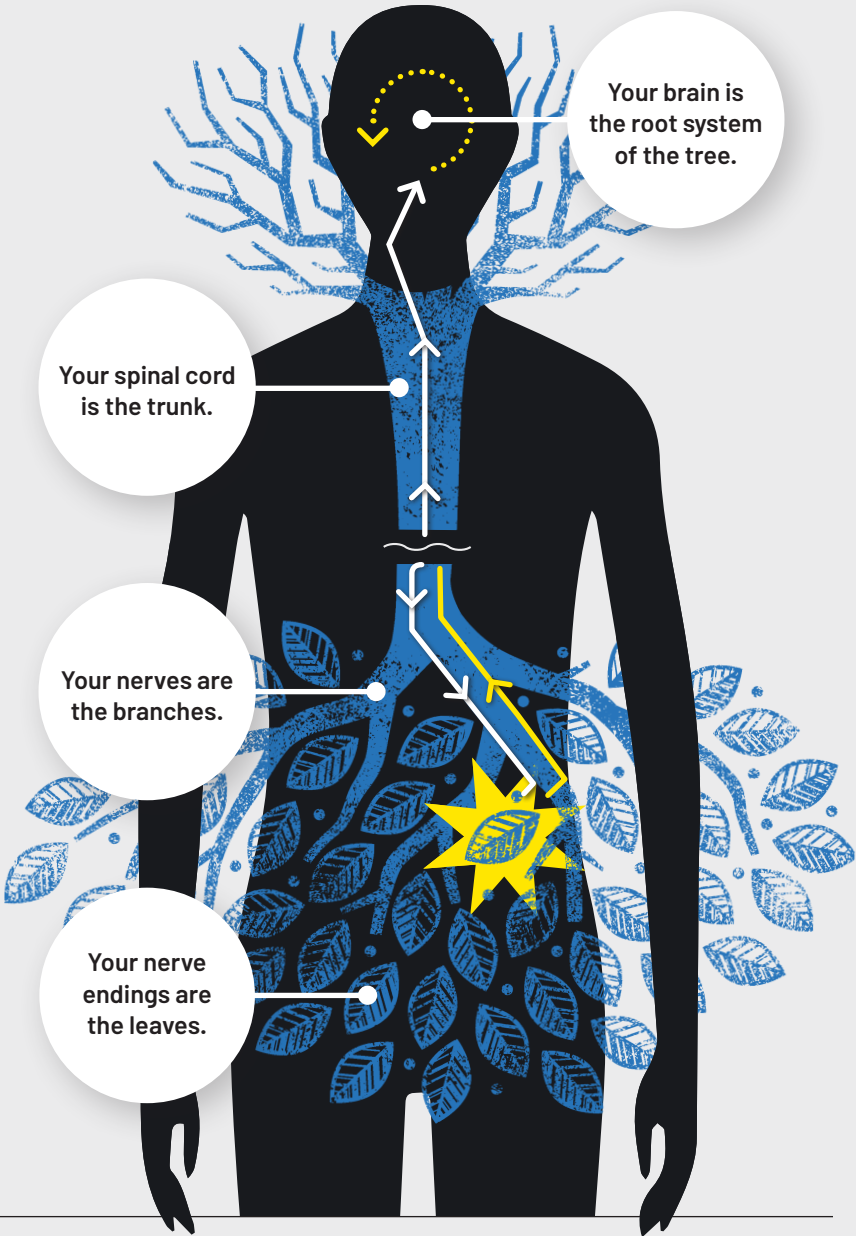
Dr. Bhatia has been working with neuroscientists at UHN to demonstrate how patients’ brains light up differently before and after pain treatments, depending on what medication is used. The patterns are as unique as each person, but Dr. Bhatia and his team have identified certain patterns that predict how well a patient will respond to a particular treatment, or if they’ll respond at all.

That type of predictive ability is the ‘holy grail’ in the pain scientific community, he says. “The right medicine for the right patient at the right time – that is really the target. So, we are making some progress. Are we there yet? No, but we will get there.” **YH**

HOW CHRONIC PAIN WORKS IN THE BODY

Dr. Anuj Bhatia likens the body’s pain circuitry to an upside-down tree.

Think of a pain signal as follows: A drop of water lands on a leaf (initial pain), which is absorbed by the leaf, flows into the branches, through the trunk and into the roots. When the **first set of neurons** carrying your pain signal reaches the trunk – your spinal cord – it reacts by sending pain-dampening signals back to the source of your pain. A **second set of neurons** carries the pain signal from your spinal cord to the brain, and a **third set of neurons** in the brain processes that pain.



DR. ANDREA FURLAN has a YouTube channel with 500K+ subscribers for people living with chronic pain.



DR. ANUJ BHATIA researches innovative approaches to chronic pain treatment, including wearable technology.

SIX THINGS YOU SHOULD KNOW ABOUT CONCUSSION



Dr. Charles Tator, Director of UHN's Canadian Concussion Centre, shares the latest in concussion research.

1

What is a concussion?

It's an extremely common brain injury that, in most cases, responds to treatment. However, significant complications can occur if it's not managed correctly, including prolonged disability and even death.

2

How can someone get a concussion?

While often associated with sports and recreation, there are other frequent causes: being hit by something on the head, motor vehicle crashes, injuries at work and domestic violence.

3

What are the common symptoms?

Only a small percentage of concussions cause unconsciousness. More common symptoms include nausea, vomiting, headaches, dizziness and memory impairment, but some only show up in certain activities, like computer use causing headaches or a feeling of imbalance.

4

What should you do if you think you or someone else has a concussion?

Seek advice from a medical doctor or a nurse practitioner. In Ontario, these are the only two types of healthcare professionals that can diagnose a concussion.

5

What happens in the brain when a concussion occurs?

Scientists at Krembil are using advanced imaging to determine if concussions can cause blood flow problems to the brain and searching for biomarkers in the blood to diagnose concussion earlier.

6

How do you treat a concussion today?

The guidelines used to recommend avoiding stimulation after a concussion, but that's changed. The current approach is to wait 12 to 24 hours, and then resume physical activity in moderation. But it's important to consult a medical professional as each patient's circumstances are unique.



IN HIS WORDS

CBC TV journalist Harry Forestell's experience with deep brain stimulation

“

FIRST NOTICED the tremors in my right hand in 2013. It was unusual, but I'm left-handed, so it didn't bother me much. The doctor, when I eventually went to see her, had two theories: a benign tremor or Parkinson's. It took two years to learn it was Parkinson's – a diagnosis confirmed after a neurologist in my home province of New Brunswick referred me to Dr. Anthony Lang, a world-renowned expert in movement disorders, at the Krembil Brain Institute.

Over those couple of years, my symptoms got worse. I had to concentrate to walk normally, swinging my arms in time to the movement of my legs, which was disconcerting. I was 53 when I first met Dr. Lang and still had a TV career ahead of me. While he was reassuring – “Don't worry, we'll get you back on air,” he told me – the symptoms continued. Medication helped, but one side effect is dyskinesia, which causes your body to twist and torque, making it difficult to stay still.

There was a way to treat these side effects: through deep brain stimulation (DBS). When Dr. Lang suggested the treatment, it sounded serious since it was brain surgery, but as my symptoms progressed, it was clear that this would be a good long-term solution. It helped that Krembil performs the most DBS treatments in the country.

With DBS, surgeons attach electrodes to the specific parts of the brain that impact movement. Extension wires are then placed under the skin behind the ear, connecting to a computer called an internal pulse generator (IPG), which creates electrical impulses that target areas of the brain controlling movement, dramatically reducing dyskinesia symptoms.

I had the six-hour surgery in October 2022, and the recovery was only three weeks. When my IPG was turned on that December, in front of a room full of clinicians, my shaking stopped completely. It was a real life-changer.

Because of Krembil's physicians and their expertise in DBS, I returned to work, and not just in the office, but in front of the camera, too. I want people with Parkinson's to know that there is hope. This is not a death sentence by any stretch. It's been a truly remarkable experience.” **VH**



DRs. ALFONSO FASANO (left) and **SUNEIL KALRA** (right) are part of a world-class interdisciplinary team at KBI that performs the highest volume of deep brain stimulation procedures in Canada.



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to hear Harry's full interview on KBI's Your Complex Brain podcast.

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