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KREMBIL
BRAIN INSTITUTE

SOLVING THE COMPLEX BRAIN

How the Krembil Brain Institute’s team-based and cutting-edge approach to tackling neurological disease is paying off.
We are here for you

Like a mosaic, the best teams are formed from unique and exquisite pieces, which, over time, come together to create a masterpiece.

We feel this perfectly describes the world-class multidisciplinary team we have built here at the Krembil Brain Institute (KBI) at University Health Network.

Our community includes many of the top thinkers and leaders in neurological research and clinical care, all under one roof.

They come to the KBI from all over the world, with one shared goal – to solve the complex brain and its diseases.

Today, nearly one in 10 Canadians live with a neurological condition such as Alzheimer’s, Parkinson’s, spinal cord injury or brain cancer. Stroke remains the third-leading cause of death, and one in four Canadians live with chronic pain.

In addition, by 2030, nearly a quarter of Canadians will be over the age of 65. As our society ages, the prevalence of these conditions will increase, causing immeasurable suffering and loss for those diagnosed and for their loved ones. That is why we need new treatments now.

In these pages, you will read about the groundbreaking research and clinical advances currently underway at the KBI, and you will hear from patients who have reclaimed their lives as a result of the care they have received here.

Solving brain disease is no easy task. It requires complete dedication, a thirst for new knowledge and a hunger to push boundaries and think creatively. At the KBI, we see science and medicine as a team sport.

We are leaders. We perform more neuro-modulation procedures, such as deep brain stimulation for a variety of disorders, than anywhere else in Canada.

We are collaborators. Our scientists work alongside clinicians, with direct access to real-time patient data. This synergistic approach helps fast-track translation of new discoveries.

We are innovators. We develop and pioneer new techniques and technologies for a vast range of neurological conditions.

Just imagine a world without chronic and debilitating neurological disorders. That is the world we envision and work toward every single day.

The finish line is in sight. We know what we need to do, and we can get there with your support.

So when you think of “brain,” think of the KBI. We are here for you.

With gratitude,

Don and Gelareh

Co-Directors, Krembil Brain Institute
Neuroscience is full of yet-to-be-solved mysteries, but one thing is for certain: Canadian brain research has partners in Dr. Kate Williams and Mr. Mark Krembil. While Mr. Krembil has been funding game-changing neuro-related science since he started the Krembil Foundation two decades ago, the organization has pushed brain research even further since Dr. Williams became its Scientific Director in 2016. “I jumped at the chance to work with Mark and the Foundation, which puts so much emphasis and value on basic science,” says Dr. Williams, who has a PhD in neuroscience with a research focus on the neural basis of age-related and neurodevelopmental vision loss. “There is so much that we still don’t understand about the brain.”

Together, Dr. Williams and Mr. Krembil are searching the country for groundbreaking research to support, much of which is happening at the Krembil Brain Institute (KBI). Unlike other foundations, which ask people to submit grant proposals for review, the duo is trying to pinpoint key areas of research by soliciting projects and then building long-term partnerships with scientists working on those areas. Their most pressing issue? Finding effective – and potentially outside-the-box – treatments for neurodegenerative diseases, such as Alzheimer’s disease. “We’re interested in different theories because this is a very complicated disease,” says Dr. Williams.

They’re particularly excited about some of the breakthroughs Dr. Donald Weaver, Research Director of the KBI, is making around small molecules. These molecules can modulate inflammation in the brain, which may help modify the disease during its different stages and alleviate symptoms in Alzheimer’s sufferers, says Dr. Williams.

The Foundation, says Mr. Krembil, has an enduring focus on the search for neurodegenerative treatments and – one day – cures. “Since its first description in 1906, there has been little progress on the treatment of Alzheimer’s disease, and that’s something that must change,” he says. “There isn’t enough Alzheimer’s research expertise in this country, but we’ve been investing in capacity through the KBI recruitments from all over the world to help change that.”

Of course, there are many other brain-related questions that must be addressed too, all of which Dr. Williams and Mr. Krembil hope to help answer – through funding and connections – as quickly as possible. “Alzheimer’s is one of the biggest global health crises we’re facing today,” says Mr. Krembil. “So timing is everything – we need to get on these things now.”
Bringing neuroscience abroad
How Dr. Mark Bernstein is helping colleagues worldwide.

Dr. Mark Bernstein smiles when he thinks back to his first global teaching experience. In 2003, he took a month-long trip to Indonesia to train residents in neurosurgery. It was 38ºC and humid every day, there was scant internet and he stayed in a tiny hotel, sharing his room with numerous beetles and moths. He was hooked.

Since then, Dr. Bernstein, a neurosurgeon and clinician investigator at the Krembil Brain Institute, who is also part of the Sprott Department of Surgery at University Health Network, has participated in more than 30 similar missions to countries around the world. He helps build capacity in neurosurgery and palliative care in countries where physicians don't have access to the same resources and infrastructure as they do here. “A lot of people would see it as charity or philanthropy. I see it as justice,” he explains.

In April 2021, the University of Toronto’s Temerty Faculty of Medicine honoured Dr. Bernstein with the Dean’s Alumni Humanitarian Award for his work training doctors in neurosurgery and palliative care. The award is given to alumni who have gone above and beyond clinical responsibilities in their work to help civic, charitable and social causes, either locally or globally.

Over 18 years, Dr. Bernstein has led teams to countries such as Rwanda, Ethiopia, Kuwait, Nigeria, Ghana, Zambia and Kenya. He often returns multiple times to continue teaching and bring new and gently used equipment to the hospitals he visits. “We often learn more than we teach,” he says. “It’s a two-way thing.”

Can cannabis treat Parkinson’s pain?

A new trial is looking at whether THC and CBD can alleviate discomfort in patients with Parkinson’s disease.

Dr. Susan Fox, Director of the Division of Neurology at University Health Network (UHN) and the Krembil Family Chair in Neurology, is fascinated with how cannabis might benefit people with Parkinson’s disease. “The areas of the brain that are involved in Parkinson's disease have a high number of receptors for cannabis,” she explains.

That’s partly why she’s leading a new study at the Krembil Brain Institute to examine the impact cannabis oil has on the pain experienced by people with Parkinson’s. Typically, the pain they live with doesn’t subside with traditional pain medications. “It’s sort of an unmet need in the field,” explains Dr. Fox, who is also part of the Edmond J. Safra Program in Parkinson’s Disease and the Morton and Gloria Shulman Movement Disorders Clinic at UHN.

Dr. Fox is testing three different cannabinoid oils from the same manufacturer, all with different ratios of delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), to see which combinations are most effective in treating Parkinson’s pain. Now that cannabis is legal, many patients have taken to treating their pain on their own, despite not knowing what doses are best or if they’re even effective. “We really don’t have any good evidence to say that this works and that it’s safe for people with Parkinson’s,” she says.

This trial will also let Dr. Fox and her team measure any side effects patients may experience. For instance, Parkinson’s patients are at risk of hallucinations, so she doesn’t want THC, the psychoactive component of cannabis, to exacerbate that issue. She hopes to publish the results by the end of the year.

Dr. Susan Fox is embarking on a groundbreaking study that looks at how cannabis oil could benefit Parkinson’s patients.
Tracking COVID-19’s toll

A new program supporting healthcare workers dealing with the pandemic is providing valuable insights into their resilience.

WHEN COVID-19 ARRIVED IN CANADA, much was still unknown about the disease. Yet, one thing was clear – healthcare workers and hospital staff found themselves in many chaotic and terrifying moments. In those early days, a team at University Health Network (UHN) asked a group of psychiatrists and psychologists to create a program, which includes one-on-one counselling, videos and infographics, to help manage the distress workers were facing.

Dr. Mary Pat McAndrews, Division Head of Clinical & Computational Neuroscience at the Krembil Brain Institute, is part of the team that created the program. She’s now studying its impact, in the hope of better supporting staff during future crises. Her team emailed a short survey to UHN clinicians, scientists and administrators to assess symptoms of distress, as well as other factors that might enhance or inhibit their ability to cope. More than 1,000 responded. “We wanted to know: what’s the normal emotional response we’re seeing right now?” Dr. McAndrews explains. “How are people situated, and how can we support them?”

Because the study took place during the first wave, the results are unique to that moment. She found that nearly half of respondents reported elevated levels of anxiety or depression, but most relied on their previous support systems to cope with the new challenges. In addition, many felt an increased sense of purpose in their work, which helped boost their resilience.

So far, the team has found that tracking down the right information and having time to access resources are barriers that need to be addressed to better handle future crises. They’re now considering another survey to see how subsequent COVID-19 waves – especially the third – have affected staff. “One thing is clear from the study,” she says. “Team UHN rose to the occasion, and that should be emphasized and celebrated.”

Next-generation researchers

The Krembil Brain Institute is a world-leading hub for up-and-coming neuroscience students from around the globe. Meet a few of our top recruits who are hoping to change the world through science.

Azin Ebrahim Amini
PhD candidate, Dr. Peter Carlen’s lab, Division of Experimental and Translational Neuroscience

RESEARCH: “I’m studying the contributing factors that regulate and redistribute potassium ion in the brain. Many neurological disorders, such as epilepsy, stroke, migraine, anoxia and cortical spreading depression, are associated with abnormally high levels of potassium ion, so it’s critical to identify the underlying processes involved in these dynamics.”

ULTIMATE CAREER GOAL: To be a pioneer in developing therapeutic approaches for potassium ion-related brain disorders.

Merrick Fallah
PhD candidate, Dr. James Eubanks’ lab, Division of Experimental and Translational Neuroscience

RESEARCH: “I’m uncovering how genetic mutations lead to CDKL5 deficiency disorder (CDD), which causes a developmental condition and epilepsy. There are no treatments for infants and children with CDD, so we want to develop novel therapeutics that target the pathological mechanisms of this disorder.”

ULTIMATE CAREER GOAL: To open a laboratory at an academic centre and continue research on pediatric epilepsy.

Cricia Rinchon
PhD candidate, Dr. Robert Chen’s lab, Division of Brain, Imaging and Behaviour

RESEARCH: “I investigate movement disorders using brain stimulation, such as musician’s dystonia, which involves involuntary muscle contractions in the hand or mouth while playing music. I’m looking for a biomarker for this condition that affects one percent of professional musicians and often has career-ending effects.”

ULTIMATE CAREER GOAL: To continue leveraging data to progress the standard of care for patients.

Camille Fauchon
Postdoctoral fellow, Dr. Karen D. Davis’ lab, Division of Brain, Imaging and Behaviour

RESEARCH: “I am working on chronic pain research, focused on sex differences associated with abnormalities in brain circuit function in chronic pain. I want to understand specific malfunctions in individuals so that personalized pain treatments can be developed and tailored to the condition of each individual.”

ULTIMATE CAREER GOAL: To establish a research lab that can predict treatment responses in chronic pain.
Strategic plan

Inside the Krembil Brain Institute

The Krembil Brain Institute is where world-leading neuroscience happens. Its vision is to transform the lives of people living with brain, spine and nerve disorders by taking an integrated, collaborative and multidisciplinary approach to clinical care, research and education. The goal? To cure and manage brain disorders, while using innovation, technology and partnerships to push the boundaries of neuroscience.

Improving patient care

Annually, the Krembil Brain Institute team provides:

150,000
Outpatient clinic visits

65,000
Neuroimaging studies

3,500
In-patient clinic visits

3,000
Neurosurgical procedures

1,100
Minimally invasive neuro-interventional procedures

Our values

We put the patient first.

We are relentless.

We are curious and push boundaries.

We work together.

We are diverse.

We respect and support each other.

We are accountable.

We invest in a sustainable future.
**Our structure**

The Krembil Brain Institute has seven highly innovative signature programs, all of which have the same 10 research priorities.

<table>
<thead>
<tr>
<th>Program</th>
<th>Count</th>
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<tbody>
<tr>
<td>Movement Disorders</td>
<td></td>
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<tr>
<td>Aging &amp; Neurodegeneration</td>
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<tr>
<td>Stroke &amp; Neurovascular</td>
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<td>Epilepsy</td>
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<td>Neuro-Oncology &amp; Skull Base</td>
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<tr>
<td>Spine, Peripheral Nerve &amp; Neuromuscular</td>
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<tr>
<td>Pain, Intervention &amp; Research</td>
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### A world-class team

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<tr>
<td>Neuroradiologists</td>
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<tr>
<td>Neurosurgeons</td>
<td>12</td>
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<tr>
<td>Neuroanesthesiologists</td>
<td>10</td>
</tr>
<tr>
<td>Neuropsychiatrists</td>
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<tr>
<td>Neurointensivists</td>
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<td>Neuropathologists</td>
<td>04</td>
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<tr>
<td>Neuropsychologists</td>
<td>04</td>
</tr>
<tr>
<td>Nursing, allied health and support staff</td>
<td>400+</td>
</tr>
</tbody>
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### Game-changing research

- **216 Researchers** focused on neuroscience
- **118** Fellows and graduate trainees
- **276** Total research staff
“I want to go out and finally enjoy the world.”

– COLIN CROXON
COLIN CROXON (centre) has struggled with seizures for nearly a decade. Thanks to deep brain stimulation technology and an expert team at the Krembil Brain Institute, he can now enjoy life again.

PUSHING THE LIMITS

With new devices, research and innovations, the Krembil Brain Institute has become a leader in the science and practice of neuromodulatory procedures.

BY DIANE PETERS

im Croxon has had many difficult days over the years, but one stands out. While at her job coaching gymnastics, she got a panicked call from her daughters, who told her to come home right away. She sped down the highway but could barely reach her house, as several ambulances, fire trucks and police cars were blocking her street. They were there to help her then-teenaged son, Colin, who’d had a severe seizure. He’d fallen down the stairs and had no vital signs until, thankfully, the paramedics revived him.

Now 22, Colin was perfectly healthy until the age of 13, when he started developing seizures. He was diagnosed with epilepsy, and the whole family has been affected by his seizures – he’s had up to 22 a day – resulting in regular calls to 911 and trips to the nearby hospital in Bowmanville, Ont. “All of us in this house have severe PTSD. We hear something drop, and we all run,” says Croxon.

To deal with Colin’s debilitating epilepsy, the Croxon family went to the Krembil Brain Institute (KBI), where they met with a multidisciplinary team of leading epilepsy experts, who determined that a vagus nerve stimulation device may be the best option for Colin. The device, which delivers electrical impulses to the vagus nerve, located in the neck, and can reduce seizures, was surgically implanted in 2017 by Dr. Taufik Valiante.

While that helped for a while, the seizures eventually restarted and the epilepsy team suggested deep brain stimulation (DBS). In November 2020, Dr. Suneil Kalia placed electrodes from a DBS device into Colin’s brain, and a controller device was put in his chest.

The result of the surgery was “mind-blowing,” says Croxon. Colin’s seizures reduced in frequency by 90 per cent. After five weeks, he was able to taper off and
then stop taking one of his strongest epilepsy medications. He now wants to train to become a mechanic. “I want to go out and finally enjoy the world,” he often says to his family.

That’s the potential impact of neuromodulation, a technology that uses electrical stimulation to alter circuit activity and reduce seizures in the brain. The KBI is already a global leader in this area, with teams working hard to push this approach to treating nerve-related conditions – especially brain conditions. “The whole field of neuromodulation is exploding,” says Dr. Valiante, Director of the Surgical Epilepsy Program at the KBI, who is also part of the Sprott Department of Surgery at University Health Network (UHN) and Co-Director of the Center for Advancing Neurotechnological Innovation to Application (CRANIA), which seeks to develop new neuromodulation technologies.

**Stimulating nerves**

“The entire body is basically run by nerves, and neuromodulation is anything that alters cell and circuit activity through a device,” explains Dr. Valiante. Often, that entails using electrodes, sometimes surgically implanted, or working from the surface of the skin to deliver an electrical impulse.

With modulation, electricity either wakes up a nerve or stops it from doing something. “When you add stimulation or electricity, especially to the brain, you either enhance electrical circuits or you short-circuit them,” explains Dr. Lorraine Kalia, a neurologist and senior scientist in the Edmond J. Safra Program in Parkinson’s Disease and the Morton and Gloria Shulman Movement Disorders Clinic at the KBI.

DBS is one of the oldest and most widely used forms of neuromodulation, pioneered in part by work done by KBI neurosurgeon Dr. Andres Lozano, but there’s also peripheral nerve stimulation, applied to areas such as the vagus nerve, plus the use of stimulation along the spinal cord. Clinicians target abnormal brain circuits, spinal cord and peripheral nerves, often with electrodes, to reduce the tremors and stiffness of Parkinson’s disease and to help other movement disorders, mood disorders, pain, spinal cord dysfunction and urological conditions.

Neuromodulation can have life-changing impacts on a range of diseases, often alleviating symptoms and allowing patients to reduce their medications. As well, Dr. Valiante says children with epilepsy are often more alert and engaged, a benefit of reduced medications but also a possible positive side effect of neuromodulation therapy. “There’s been arguments that brain stimulation may have some pro-cognitive effects,” he says.

Currently, half of all DBS implants in Canada are performed at the KBI, but that represents just one aspect of its wide-ranging neuromodulation work. Its clinicians and researchers are reimagining the field to offer more effective treatments and invent game-changing devices – all of which are helping doctors treat nerve-related health conditions and symptoms.

**A multidisciplinary team**

One way the KBI is leading the charge is by creating multidisciplinary teams that work together to study and improve upon neuromodulation techniques, says Dr. Valiante.

Typically, different experts perform neuromodulation on different parts of the body. They often work separately and seldom interact. Dr. Alfonso Fasano, a neurologist and clinician investigator at the KBI and Chair in Neuromodulation and Multidisciplinary Care, is creating an interdisciplinary neuromodulation unit at the KBI. The unit will allow experts such as neurologists, pain specialists and urologists to share innovations, try new approaches to treatment and offer comprehensive training. “We want to look at...
neuromodulation as a whole,” he says. “This is something that will be unique worldwide. We are trying to change the field.”

Dr. Fasano believes this new unit will help care teams across the KBI better understand neuromodulation and—importantly—stop people from thinking of it as a last-resort treatment. “It’s been proven that if you do a treatment like DBS earlier, it’s better for the patient’s quality of life,” says Dr. Fasano. “They don’t lose their job. They keep their friends. If you wait too long, you treat patients whose conditions are too advanced, and then surgery becomes too risky.”

Making smarter devices
A few months after Colin got his DBS device, several days of stormy winter weather triggered seizures. Fortunately, Colin’s revolutionary device records brain activity data and sends it to a dedicated cellphone in his home. His team at the KBI then downloads the data and compares it to his seizure activity, using it to create a customized setting to better manage his condition.

This kind of monitoring is incredibly innovative—it wasn’t long ago that brainwave monitoring could only happen during brain surgery. Now, clinicians can peer into the inner workings of the organ anywhere and at any time. And the technology is only getting more sophisticated. Devices are now starting to sense when a seizure is about to happen, while future tech could stop seizures before they occur. “The next generation of devices will have the capacity to sense what the brain state is and respond,” adds Dr. Suneil Kalia, a neurosurgeon and part of the Sprott Department of Surgery at UHN.

“We’re going all the way from the basic science to developing the devices and then implanting the devices. We’re building an ecosystem here to do it all.”

– DR. TAUFIK VALIANTE

The KBI researchers are a big part of this promising future. Dr. Valiante has a smart device in the prototype phase called a neural interface processor for brain-state classification and programmable-waveform neurostimulation (NURIP). It uses an implantable computer chip that can detect an impending seizure and deliver stimulation to stop it from occurring. The system uses artificial intelligence to learn when and where in the brain a patient has seizures, and uses stimulation to shut them down before they happen.

Inventing more devices like NURIP is a key goal at the KBI. “We’ve been leaders in using commercial devices. We’re now motivated to create that next generation of devices,” says Dr. Valiante.

He helped launch CRANIA in 2017 for this reason. It’s a partnership between the KBI, Toronto Rehab at UHN and several faculties at the University of Toronto. Dr. Valiante says having top equipment and expertise from across UHN will help Toronto become a leader in creating the next generation of neuromodulation devices, software and spinoff companies.

Preventing disease
Drs. Lorraine and Suneil Kalia, a husband and wife team, are also looking at how neuromodulation might be used to prevent diseases from progressing in the first place. The Kalias are developing drugs to stop cell death in Parkinson’s, and neuromodulation may be able to do this, too. “In stimulating brain circuits, we might be able to affect molecular pathways in the brain cells of patients with Parkinson’s to prevent those cells from dying,” says Dr. Lorraine Kalia.

While this research is still very preliminary, she explains, “if we could use stimulation for prevention, that would be an even stronger indicator for us to think about using stimulation earlier.”

By treating patients with neuromodulation for a wide range of conditions, inventing the next generation of smarter and more responsive devices, and undertaking basic research to actually prevent illness, the KBI has entrenched itself as a world leader in this growing field.

“We’re going all the way from the basic science to developing the devices and then implanting the devices,” says Dr. Valiante. “We’re building an ecosystem here to do it all.”
“I genuinely believed that I was about to die.”

Patients with trigeminal neuralgia, like Joshua Johnston, often suffer excruciating pain. Dr. Mojgan Hodaie, a neurosurgeon and scientist at the Krembil Brain Institute, found a way to help.

BY GLYNIS RATCLIFFE
t was the dead of winter when 21-year-old Joshua Johnston first experienced a cranking shock of pain across one side of his face. He was walking down a street in Elliot Lake, Ont., when, he says, "I thought I had been shot. It came out of nowhere and dropped me to the ground." After writhing in pain on the sidewalk for what felt like an eternity, he dragged himself into the emergency room, which, thankfully, was across the street. "I genuinely believed I was about to die in that moment," he says.

Fortunately, it only took a few days to determine the source of his pain: trigeminal neuralgia, a chronic facial neuropathic pain linked to the trigeminal nerve. It’s a rare disease — about 12 in 100,000 people are diagnosed with it each year — and it often goes undiagnosed or gets mistaken for other illnesses.

Over the next 16 years, Johnston tried anticonvulsants and barbiturates to help manage his pain, both of which he reacted poorly to, and had three major surgeries, each of which gave him less than a year’s respite from the constant burning and taser-like jolts in his jaw and cheek. "Everything was deteriorating," says Johnston, a firefighter who has since become a leading fire scientist after throwing himself into his work as a means of coping with the agony.

The disease is so devastating because this nerve supplies sensation to different areas of the face: the lower jaw, teeth, lips, cheeks, forehead, scalp and eyes. The classic presentation of trigeminal neuralgia is recurring flashes of excruciating pain in some or all of these areas, lasting as long as two minutes. The pain can come from actions as simple as brushing your teeth or smiling, or even a gust of wind. Neuropathic pain, which is caused by damage or injury to the somatosensory system that regulates sensation in the body, is generally hard to treat because, like all pain, it is subjective and not easily quantified or measured.

Thankfully, Dr. Mojgan Hodaie, a neurosurgeon and scientist at the Krembil Brain Institute (KBI) and the Greg Wilkins-Barrick Chair in International Surgery, who is also part of the Sprott Department of Surgery and Surgical Co-Director of the Joey & Toby Tanenbaum Family Gamma Knife Centre at University Health Network, is changing that with her groundbreaking work.

Innovative research

Before Dr. Hodaie began studying this disease, most research centred around understanding the blood vessels that reside close to the trigeminal nerve and often compress it. While they do play a role, Dr. Hodaie has focused on studying the nerve itself, since it is the key player generating the pain.

She’s developed and applied novel MRI techniques that allow researchers to zero in on fibres in the brain to investigate both the properties of the trigeminal nerve and the pathway of that nerve in the brain. Dr. Hodaie’s technique mixes anatomical images with colour to highlight the normally black, white and grey fibres. This makes it easier to see which direction they are travelling in. "I use this technique to investigate what’s happening at the level of the trigeminal nerve itself and whether the fibres are altered or abnormal in the setting of trigeminal pain," explains Dr. Hodaie.

With advanced structural imaging, Dr. Hodaie — who is one of the world’s top experts in this disease and one of the few surgeons in Canada who focus on surgery for the treatment of trigeminal neuralgia patients — can develop a better understanding of what pain looks like in the brain. "It’s not just that the nerve changes; there’s actually signatures of pain in key areas of the brain," says Dr. Hodaie, who has performed well over 1,000 procedures for this disease.

Her goal is to give patients a better understanding of how likely it is they will benefit from surgery, including microvascular decompression or stereotactic radiosurgery using Gamma Knife, which uses focused radiation beams on the trigeminal nerve to treat the pain.

Understanding pain

In 2020, Johnston, who had been experiencing hundreds of shocks a day, was referred to Dr. Hodaie. By then, he was out of options. "I had no hope until I met her," he says.

She offered him a different approach — neuromodulation using fine electrodes under the skin, which mitigates the nerve’s pain signals through the implantation of a programmable device in the body — and it changed his life. Pain still exists, but he can dial it down to a manageable level with what’s essentially a remote-controlled pacemaker — except the device is pacing his nerves, not his heart.

Dr. Hodaie is now training neurosurgeons at the KBI and around the world, as well as exploring the use of machine learning to study larger and more detailed subsets of brain images. Through this research, she and the team at the KBI will have an even greater capacity to change lives.

They’ve certainly changed Joshua Johnston’s life. Now 37, he can finally carry his four-year-old without worrying about dropping him, and his kids call him “robot daddy” due to his neuromodulator device. “I feel like I woke up out of a coma,” he says. “There are so many aspects of my life that I never realized had been compromised by the pain.”
Innovative approaches to chronic pain

The Krembil Brain Institute’s chronic pain experts are using novel treatment approaches – and returning people to meaningful lives.

BY ANNA SHARRATT

If anyone knows how difficult it can be to deal with unrelenting chronic pain, it’s Paul Ross, a Toronto resident with colitis and Crohn’s disease who has been dealing with extreme abdominal pain for more than two decades. “It’s excruciating,” says Ross, who suffers from intestinal blockages multiple times a month. “There were times I didn’t want to live.”

Since 1989, Ross has undergone 12 operations. He has an ileostomy bag and, at times, has needed tube feeding. To control his pain, he’s relied heavily on powerful opioids. Unfortunately, relief came at a terrible cost: the side effects impacted his day-to-day life. “My kids were afraid that my grandkids would see me injecting myself,” he recalls. “Though everything was prescribed by my doctors, I had become a drug addict.”

The turning point came in 2016, when Ross developed sepsis, a life-threatening full-body infection. After an operation to remove damaged tissue, he was given two fentanyl patches, in addition to his self-injected hydromorphone for pain relief. That was when he realized he couldn’t live without powerful painkillers – and something had to change. “I told my doctor, ‘I’m not leaving here until I get a referral to someone who can get me off these drugs,’” he says.

His doctor knew who could help: Dr. Hance Clarke, a clinician investigator at the Krembil Brain Institute (KBI), an anesthesiologist and Director of Pain Services at the Department of Anesthesia and Pain Management and the Director of the GoodHope Ehlers-Danlos Clinic at Toronto General Hospital. That referral would transform his life.
A holistic approach

Dr. Clarke is a leading expert in opioid alternatives. He uses holistic therapies, such as mindfulness training, acupuncture, yoga, massage therapy, exercise and cannabidiol (CBD, found in cannabis), in addition to, or in lieu of, the powerful painkillers chronic pain patients take. These integrative approaches teach patients alternative strategies to control how they handle and experience their pain. “Your brain is as strong as your medications,” says Dr. Clarke. “We can teach patients how to live with their pain.”

In 2014, he created the Transitional Pain Service (TPS) at University Health Network (UHN), a one-of-a-kind centre that’s revolutionizing pain management by helping patients manage their pain and by preventing the development of persistent opioid use and misuse. Patients are either directed to the clinic after surgery – they may have pain out of the norm and are prescribed opioids – or are already taking medications and need guidance regarding pain and medication management.

Many doctors still prescribe opioid medications after routine medical procedures and, for those who go on to develop a problem related to their care, the TPS enables support during this challenging time. One in 10 patients on high-dose opioids eventually struggles with an opioid misuse problem. “We’ve created a template for institutions to help these patients earlier in their post-operative pain trajectory so they don’t go on to develop an opioid use disorder,” says Dr. Clarke.

From April to September 2020, 3,351 Canadians died from opioid toxicity, a 74 per cent increase from the six months prior, according to Health Canada. The increased use of fentanyl-like substances continues to be the main culprit for these deaths, and patients on high-dose opioids need a safe place to turn. The TPS practises a non-judgmental approach that supports some of the most vulnerable patients.

Ross’ withdrawal was challenging. He went to the hospital for medical support, but when he got there, he was too weak to stand. “I was constantly throwing up,” he says. “Dr. Clarke carried me to the bathroom in his arms.” Dr. Clarke prescribed him suboxone, an opioid agonist treatment medication, which helps relieve the debilitating symptoms of withdrawal. He also checked in with him constantly, even phoning him at home. Just one day after starting suboxone, Ross could see progress. “I woke up, showered and suddenly realized: not once did I reach for my syringe,” he says.

In the weeks that followed, Ross tried acupuncture, yoga and therapy under Dr. Clarke’s guidance. But it was the centre’s mindfulness program with Dr. Aliza Weintrab – using breathing exercises and guided imagery to bring awareness to the present moment – that gave him the tools to start his new life. “Now I can respect my pain – I’m not scared of it,” he says.

Drug-free digital advances

In addition to employing holistic approaches, the TPS launched a digital health app to help patients monitor pain symptoms and improve their contact with clinicians. Patients rank their pain scores out of 10, document their emotional reactions and provide summarized reports of their progress. “People who used the app reported a reduction in anxiety and catastrophizing,” says Dr. Anuj Bhatia, a clinician investigator at the KBI and Director of Anesthesia and Chronic Pain Clinical Services at UHN.

There have also been advances in drug-free techniques such as neuromodulation, which is the use of devices that generate electrical currents to override pain signals from nerves. Patients can control the intensity of the device, depending on their pain. “It is quite an amazing therapy, as it allows patients to come off opioids,” says Dr. Bhatia, adding that other drugs, such as ketamine, an anesthetic medication, are also being explored as a way to help patients with long-term neuropathic pain.

Patients aged 16 to 80 have benefited from these implants at the Neuromodulation for Pain Program at UHN. Other image-guided interventional procedures performed at UHN have also helped alleviate certain types of pain originating in the spine or the nerves. For instance, in 2019, Terie Elliott, a patient in the program, received Canada’s first battery-free peripheral nerve stimulator to alleviate intractable foot pain. She’s now walking, bending and moving.

Physicians, nurses, psychologists and physical therapists in the Comprehensive Integrated Pain Program at UHN, in collaboration with pain programs at Sinai Health and Women’s College Hospital, have also created clinics to address other kinds of pain, whether it’s related to joints and muscles, headaches and facial pain, cancer or pregnancy.

As for Ross, he is no longer on any pain drugs and practises mindfulness whenever he experiences intestinal blockage. “I was the world’s greatest skeptic,” he says. “But it’s unbelievable what mindfulness has done for me. I have my life back.”
The CODEBR

Dr. Andres Lozano is using deep brain stimulation to help treat Alzheimer’s and Parkinson’s disease.

Dr. Carmela Tartaglia wants to detect neurodegenerative diseases sooner by improving diagnostic methods.

Dr. Gabor G. Kovacs is examining how neurodegenerative diseases impact the human brain at microscopic and molecular levels.

Video Link: Deep Brain Stimulation for Alzheimer’s (TVO)

Video Link: A more accurate diagnosis for dementia

Video Link: Movement Disorders Speaking Series
Neuroscientists and clinicians at the Krembil Brain Institute are learning more about neurodegenerative diseases like Alzheimer’s and Parkinson’s, one insight at a time. **BY ELIZABETH CHORNEY-BOOTH**

**VIDEO LINK:**
The impact of Alzheimer’s and dementia

**VIDEO LINK:**
The gut-brain connection

**DR. MILAD LANKARANY**
is using computational neuroscience to help researchers and clinicians better understand the workings of the brain.

**DR. OLGA ROJAS**
is studying the relationship between inflammation and neurodegeneration.
there are few medical diagnoses more terrifying than diseases that affect the brain. Whether it’s Parkinson’s disease, Alzheimer’s or another form of dementia, or the long-term effects of concussion, neurodegenerative diseases directly impact how we identify as human beings. Everyone dreads the thought of losing brain function and, especially, their memories. Worst of all, there is no known cure or effective treatment for most of these disorders.

At the Krembil Brain Institute (KBI), some of the world’s top medical minds have dedicated their careers to cracking neurodegeneration’s still-elusive code. They’re working on innovative ways to diagnose disease earlier, experimenting with novel treatments like electrical stimulation, employing advanced computational science to study the impact of surgery on the brain and more.

No one is looking for band-aid solutions. Instead, they want to develop a comprehensive understanding of neurodegenerative diseases and how they can be prevented, treated and eventually cured. “We’re not going for the low-hanging fruit. We’re going for the apple at the top of the tree,” says Dr. Donald Weaver, Research Director of the KBI. “We’re going to have to step on some branches we haven’t trodden upon before.”

**Better diagnoses**

One challenge is that different neurodegenerative diseases have similar symptoms. If a patient complains about forgetfulness or motor control problems, diagnosis is difficult until symptoms progress. Since many researchers believe early diagnosis can give clinicians a better chance of treating disorders like Parkinson’s and Alzheimer’s, as well as the fallout of repeated concussions, developing new diagnostic methods is a potential game-changer.

Dr. Carmela Tartaglia, a neurologist and clinician investigator at the KBI who studies both concussion and neurodegenerative issues, wants to detect cognitive impairment problems earlier, while also using biomarkers to generate more precise and individualized diagnoses. One challenge with that is concussions and other brain-related diseases can’t be properly diagnosed until after death. “What we’re striving to do is to bring precision medicine, the kind we have come to accept with cancer and heart disease, to neurodegenerative diseases,” says Dr. Tartaglia, who is also the Marion and Gerald Soloway Chair in Brain Injury and Concussion Research. “We want to talk to patients about the cause of their dementia and give them a specific diagnosis, because different kinds of dementia have very different prognoses.”

**Surgical successes**

There may be no cure for most neurodegenerative diseases, but the KBI is working on developing life-altering treatments that can help with symptoms, particularly for Parkinson’s disease. Dr. Andres Lozano, a neurosurgeon and senior scientist at the KBI, and the R. R. Tasker Chair in Stereotactic and Functional Neurosurgery, is a pioneer in the use of deep brain stimulation (DBS), which can dramatically ease the symptoms of a number of neurological disorders, including Parkinson’s and Huntington’s diseases. A recent study showed an 88 per cent accuracy in optimizing DBS stimulation settings, through combining fMRI results, which show metabolic activity in the brain, with machine learning techniques. “The hope is that this could facilitate more customized treatments for our patients,” says Dr. Lozano, who is also part of the Sprott Department of Surgery at University Health Network.

While DBS, which uses electrodes to stimulate nerves within the brain, is a well-established treatment for Parkinson’s, Dr. Lozano is leading a significant third-phase study examining its potential for managing Alzheimer’s disease. “This is a very different approach to treating Alzheimer’s,” he says. “Most Alzheimer’s research involves trying different drugs. This is something different, where we’re changing the activity of the brain using electricity.”

**The brain, from every angle**

When a breakthrough happens, it’s going to
be because of the KBI’s multidisciplinary and highly innovative approach to research.

For instance, Dr. Gabor G. Kovacs, a neuropathologist and senior scientist at the KBI, works with the donated brain tissue of deceased patients. This allows clinicians to see first-hand how Alzheimer’s, Parkinson’s and a wide spectrum of neurodegenerative diseases affect the human brain at the microscopic and molecular level. Dr. Tartaglia can tell how her biomarker research correlates to what is observed in the brain, while Dr. Lozano can examine how electrical stimulation affects brain tissue. There’s also important work being done in the Edmond J. Safra Program in Parkinson’s Disease, led by Dr. Anthony Lang, the Lily Safra Chair in Movement Disorders.

Dr. Kovacs believes the communication and complementary research between clinical and lab-based scientists are some of the keys to the KBI’s success. “Neurodegenerative diseases really need to be approached with this harmonized team strategy,” he says.

**Connecting the body with the mind**

This is why the KBI has recruited leading neurologists, neurosurgeons and specialists to the team, each of whom brings a unique perspective to brain research. Dr. Olga Rojas, an immunologist and scientist, for example, is a recent addition to the team whose background is the gut microbiome.

Dr. Rojas studies the relationship between inflammation and neurodegeneration, particularly how our bodies’ responses to bacteria and other factors that cause inflammation might contribute to Alzheimer’s and Parkinson’s diseases. It’s a growing area of study that may help researchers connect disorders of the brain with other issues in a patient’s body. The assertion isn’t that inflammation is the sole cause of neurodegenerative disease, but that it’s one part of a larger puzzle. “We’ve shown a link between the immune cells that develop in the intestine, from bacteria that grow in the gut, and inflammation in the brain,” she says. “We’ve been able to learn how this affects the progression of diseases like multiple sclerosis, and now I’m trying to translate that knowledge to see if it applies to neurodegeneration.”

**Cutting-edge approaches**

Basic science and clinical research are key tools in the fight against neurodegenerative diseases, but the KBI also takes some less conventional approaches to supplement more traditional methods. The KBI is a leader in computational neuroscience, a field that uses mathematical tools to better understand brain function.

Experts like Dr. Milad Lankarany, a scientist at the KBI, use computational neuroscience to help researchers like Dr. Lozano gain a better picture of how his surgery methods affect brain function. “We use data that clinicians and neurosurgeons have recorded from their patients to develop models that can show us how a neurodegenerative brain works differently,” Dr. Lankarany says.

Meanwhile, Dr. Maurizio De Pittà, also a scientist at the KBI, is using computational neuroscience to study neuron-glia interactions, particularly in relation to Alzheimer’s disease. “My models aim to diagnose pathological scenarios and guide therapeutic interventions,” Dr. De Pittà explains.

All of the KBI’s research projects and methods overlap and intersect to form a bigger picture of how these diseases affect the brain and how they might be treated, leading to many significant behind-the-scenes breakthroughs. While we’re more likely to see a series of treatments than a miracle cure, real advancements are around the corner as long as scientists continue to get the support and funding they need to do this monumental work.

“We must understand that this is doable,” Dr. Tartaglia says. “Look at cancer. If cancer research had stopped because they didn’t yet have cures, we wouldn’t have any of the life-saving treatments we do today. We need to make that same investment in brain disease research that’s led to so many cancer breakthroughs. We’ve already come a long way, but with the right resources in place, we’ll be making real headway.”
A radical method for treating spinal cord injuries

How a groundbreaking procedure is helping injured patients move again.

BY TAMAR SATOV

In November 2017, Analynne Salas and her partner, Domingo Blanquera, pulled into a parking lot in Toronto's east end, on their way to an appointment to discuss their mortgage. Blanquera helped Salas out of the car, as she’d been experiencing numbness and weakness in her limbs for months. But as they walked hand in hand, Salas suddenly lost sensation in one leg and fell onto her back before he could catch her. “I was conscious, but I couldn’t move anything except my eyes and my mouth,” recalls Salas, who’s now 46. “I was scared. I thought I was going to die.”

Blanquera called 911, and tests performed at a nearby hospital determined that her spinal cord was badly injured, leaving her paralyzed with no movement from the shoulders down. The cord’s bruising and internal bleeding were a result of not just the fall but also a pre-existing condition called degenerative cervical myelopathy (DCM), which is the most common cause of spinal cord injury in the country. The disorder, which affects two per cent of Canadians and leads to a 1,000-fold increased chance of spinal cord injury (SCI), turned the ligaments in her upper and middle spine into bone. That ossified tissue then squeezed her spinal cord, which caused the numbness and unstable gait that precipitated her fall.

To have any hope of using her arms and legs again, Salas needed immediate spinal decompression surgery, a delicate procedure in which those ossified ligaments would be removed, preventing further damage to blood vessels and nerve cells.

Her healthcare team made a key decision that would vastly improve the trajectory of her recovery: they transferred her to University Health Network’s (UHN’s) Toronto Western Hospital under the care of Dr. Michael Fehlings, a neurosurgeon and senior scientist at the Krembil Brain Institute and the Gerry and Tootsie Halbert Chair in...
Neural Repair and Regeneration, who is also part of the Sprott Department of Surgery at UHN.

**Time is spine**

Dr. Fehlings was among the first clinician-researchers to identify the benefits of early decompression surgery. A study he published in 2012 compared patient outcomes among 313 SCI patients in six centres across North America. It showed that the odds of having significant neurological improvement six months after injury was three times higher for those who had spinal decompression surgery within the first 24 hours, compared to those who had surgery later. “The approach I took was considered to be very radical at the time,” he says.

Dr. Fehlings then undertook a more detailed study, published last December, which analyzed data from four previous studies that included 1,548 SCI patients after surgery. At one year post-injury, patients who had the procedure within 24 hours showed greater improvement in all motor scores tested. Plus, the earlier patients received surgery, the better their recovery. “The study definitively showed for the first time that ‘time is spine,’” says Dr. Fehlings. “Providing surgical decompression early, within 24 hours, is mission critical.”

**Putting research into practice**

When Salas arrived at Toronto Western around midnight, Dr. Fehlings had to act fast. He rushed in to assess her at 2 a.m. and had her in the operating room by 6 a.m. – a mere 16 hours after her fall.

He cut into her back to remove the thickened tissue and bone that was narrowing her spinal canal. The compression on her cord was so severe he had to take out much of the arch of her upper spine and reconstruct it with screws and rods made of titanium. “She’s now the bionic woman,” quips Dr. Fehlings, underplaying the remarkable achievement of the painstaking six-hour surgery.

After initially recovering in the intensive care unit, Salas was admitted to the general ward for spinal patients under the care of a specialized team of nurses, occupational therapists, social workers, physiotherapists, spine fellows and residents, in addition to Dr. Fehlings. “Almost every organ system is affected with spinal cord injury, so a multidisciplinary team approach is required,” he says.

Advance practice nurse Rosalie Magtoto collaborates with the multidisciplinary team in the unit and ward, which provides care for patients. She’s been working with the spine team, part of the neurosurgical group, for the past 17 years – attending interdisciplinary rounds and family meetings to fulfil the care needs of patients and their families.

Importantly, she is a reassuring support for those whose lives have been upended. “When you have a spinal cord injury, there is a fear of the unknown. You don’t know if you’re going to walk again or if you’ll be able to return to your job, and the quality of a patient’s life is affected,” she says.

**Recovery milestone**

After spending about two weeks in the unit, Salas managed a slight stir in one of the fingers in her right hand when Dr. Fehlings held it. “He said to his nurse, ‘This is very promising progress. Let’s get her to rehab!’” recalls Salas.

Magtoto also remembers that moment: “When she started showing improvement, it was very gratifying for all the participants in her care.”

Salas then went to Toronto Rehab’s Lyndhurst Centre and was upright and standing within three weeks. By the time she left in February 2018, she was on the move with a walker, and she continued physiotherapy as an outpatient for six more months.

Today, Salas has regained nearly all of her normal function, aside from not being able to move her neck fully from side to side. And while it’s possible she may someday require surgery on her lower (lumbar) spine – as do 20 per cent of patients who have DCM – research into new therapies and medications offers additional hope for those with an SCI.

For example, Dr. Fehlings recently completed a Phase 3 randomized control trial to see if Riluzole, a sodium channel blocker, can improve the recovery of patients with a traumatic SCI when given within 12 hours of injury. He expects to publish the results later this year.

“I can’t believe what science can do. I thought that was the end for me,” says Salas, who is grateful to be there for her family, including her three kids, aged six, 17 and 20. “I appreciate what Dr. Fehlings did for me. His team is amazing.”

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**Screws and rods made out of titanium are used to reconstruct the spine during decompression surgery.**
AN ALTERED LIFE

At age 51, Marianne Fedunkiw suffered a series of devastating strokes, but she got her life back thanks to Dr. Aleksandra Pikula, a stroke neurologist at the Krembil Brain Institute, and the team at Toronto Rehab, including occupational therapist Jessica Galbraith. Here is her story.

BY WENDY GLAUSER

VIDEO LINK: Krembil Minute – Stroke
**MARIANNE FEDUNKIW:** I had my first ischemic stroke when I was 34, and I bounced back really quickly. I was only in the hospital for a few days. I thought it was a fluke because I had none of the risk factors. A few months later, I went on to finish my PhD and pursue an academic career.

Then, in 2016, my husband and I spent six weeks back in Oxford, England, where I had finished my postdoctoral fellowship years before. I was 51 and working on my second novel. I was cycling to a friend’s for dinner when I had to stop. I had a headache, with a pounding so severe it felt like a stake was being driven through my head. I texted my husband and he met me with an Aspirin, and that helped. I even got through the dinner.

We didn’t realize I was having a stroke so it was only when a friend insisted, that I went to the hospital in Oxford. After an overnight stay, I was discharged. We were due to fly to Toronto a few days later, as my research contract was up. The day after we returned, I went to the emergency department because I still had a bad headache and I was spending a lot of time sleeping. I woke up in the stroke unit of Toronto Western Hospital. I later found out that this time I had had both a hemorrhagic and an ischemic stroke. About half of hemorrhagic strokes are fatal, so it’s a miracle I survived.

**DR. ALEKSANDRA PIKULA:** I met Marianne briefly on admission, then followed her for about 90 days after her strokes, which is standard practice. During her hospitalization, Marianne spent time in the intensive care unit. But when I saw her, she had already completed in-patient rehab, she was able to walk and her language had recovered. Typically, at this point most patients would be discharged from our clinic. The stroke neurologist would educate the patient on what to do to avoid a second stroke, such as addressing common risk factors (high blood pressure, diabetes) and engaging in healthy lifestyle choices. Then they’re back to their family physician for ongoing followup.

However, what we see is that such short interactions with patients are a real problem. Stroke is a life-changing experience, and even if a patient recovers from their physical deficits, there are many emotional issues to deal with as well. A stroke can have a major impact on a person’s well-being at any age, but for people under 65, like Marianne, a stroke can be truly devastating. Post-stroke recovery may take years. Many patients feel they need to learn how to navigate a new norm, as they try to get back to their careers, their relationships, their lives. At the same time, many patients are responsible for taking care of young children or elderly parents. Yet, despite no true physical disability, they may have “invisible” deficits that will not allow full engagement. The research shows that 30 to 40 per cent of younger stroke patients will experience cognitive dysfunction post-stroke, such as difficulty with multi-tasking and attention, and up to 80 per cent have psychosocial issues, like depression and anxiety, or the feeling of ongoing stigma and loss of self-identity. Many aren’t able to go back to work right away, or ever, so there’s a huge economic cost, but also a personal and societal cost. It’s a lot to expect family doctors to manage these complex issues alone, so we have to shift our focus to thinking of stroke as a chronic disease rather than an acute one.

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**Act FAST!**

The acronym FAST is used by numerous organizations around the world to help people understand and detect stroke symptoms.

- **F**ace: Is it drooping?
- **A**rms: Can you raise both?
- **S**peech: Is it slurred or jumbled?
- **T**ime to call 911 right away.
Providing support to younger patients

DR. PIKULA: Stroke in younger adults and patient-reported outcomes are not well understood or commonly studied. My team and I are conducting a very important study that examines the long-term psychosocial and occupational needs of younger stroke patients, with an emphasis on our patients’ lived experience. We’ve gathered data on around 100 patients, using tools that measure a variety of aspects of quality of life, including their mental health, social supports and treatment preferences. Only 25 of these patients went back to work full time. We’ve also conducted in-depth interviews with about a quarter of the patients in the study to better inform how we can care for patients after stroke in a more holistic manner and help them reintegrate back into their personal and professional activities. More importantly, we are in the process of developing an intervention that will be further tested to examine how to help these patients adopt a proactive self-management approach to lifestyle changes, thus limiting the chances of stroke recurrence (which is high in this population group, given their expected longer lifespan post-stroke).

MARIANNE: When I first spoke with Dr. Pikula, I was breaking down a lot. She connected me to a psychiatrist, Dr. Kathleen Sheehan, who works with relatively young people with chronic illness. Dr. Sheehan helped me work through the grief related to the death of my father and the loss of the academic career I was hoping to have. In my life at Oxford, I was always meeting new people and striking up interesting conversations. After my stroke, I knew I couldn’t pursue my dream job there. I can’t multi-task anymore, and handwriting is something that hasn’t come back, though I’m still able to type. For me, my career is my identity. If I don’t have my career, then who am I? The mental health implications of a post-stroke world can be devastating.

Embracing a new life

DR. PIKULA: At our stroke program for younger adults, called SIYA, we follow patients for years after a stroke. I see them every six months, and our clinic readily connects them to rehabilitation, psychiatry, nutrition and a range of other services that are closely integrated. At University Health Network, about 15 per cent of people recovering from stroke are under 50, while 30 per cent are below the age of 65. This population group is often in a peak professional position. Many have families, young children or elderly parents to take care of, and their identity is interconnected with professional achievements and life satisfaction, so they need a strong support system. I try to guide them into adapting their career expectations and rediscovering themselves. For example, one of my patients was a business executive, and now she is working part time as a business consultant. She still has that purpose through her work, but she’s contributing in a different way. Many patients started a new career or even began volunteering to rediscover their purpose. It’s the same with Marianne. She’s finding ways to bring her research and passion for writing back into her life, yet on her own terms.

Better brain-saving operations

The Krembil Brain Institute is pushing the envelope to help more stroke patients.

Until recently, there wasn’t much clinicians could do to treat major strokes. Blood thinners could help break up small clots, but it was hard to treat big ones. Then, in 2015, results from a breakthrough endovascular therapy (EVT) trial were released that forever changed how strokes get treated. With this therapy, a catheter is inserted into the groin or wrist and carefully moved through the blood clot in the brain. Then, a wire with a stent on the end is pushed through the tube. When the wire reaches the clot, it “grabs” it and pulls it out. At first, major stroke organizations only recommended EVT for strokes caught within six hours and in large veins. In the years since, however, clinicians at the Krembil Brain Institute (KBI) have increasingly pushed those limits. “We’re moving into new frontiers,” says Dr. Ronit Agid, a neuroradiologist and clinician investigator at the KBI. “At first, we would only go if it’s a large vessel; now we go into vessels that are one millimetre in diameter.” So long as imaging shows the area near the clot still has some blood circulation, clinicians can operate up to 24 hours after a stroke. The new treatment possibilities mean more brain-saving operations than ever before, especially at the KBI, which is
MARIANNE: Dr. Pikula has helped me realize I have worth outside my career. It’s very subtle, how she does it. When she talks to me, I don’t feel like she pities me. It’s like she’s catching up with a former colleague who has just taken a different path. She’s helped me accept that I needed to give myself time. In stroke recovery, often the brain is ready to go off and resume life as normal. But then you can be hit by fatigue – you might even fall asleep in the middle of a conversation. So you really need to relearn how to “be,” and in my case, I needed to consider “who” I could become.

DR. PIKULA: We’re still analyzing the results of our study of younger stroke survivors, but one theme we’ve seen is that they need long-term and comprehensive supports in many aspects of their recovery. Many express a need to have a health navigator who is specialized in stroke to help them access services in the community, like nutritional programs, mental health services and classes like yoga, where people can engage socially with less pressure, that are geared toward younger adults with similar experiences. Medications help, but we have to work on complementary tools as well, assisting patients with improving their lifestyle. Stress, sleep and diet are really important for the brain to recover, as well as to prevent another stroke. Based on this study, we’re in the process of designing a program to better meet the needs of young stroke patients, and we recommend governments fund such programs. It costs money, but when you consider the impact on someone’s long-term mental and physical health, and for our society as a whole, it’s worth it.

JESSICA GALBRAITH (OCCUPATIONAL THERAPIST AT TORONTO REHAB): When I met Marianne, she suffered from brain fog, what she described as “getting stuck.” I helped her find ways to conserve her energy and stay focused. We used an approach called goal management training, where we would break down her writing goals into smaller chunks and plan how she could work on the steps. We worked on schedules where she would write for short periods of time, not hours like she did before. And we would build on that, day by day.

We want to support people in achieving their goals of returning to work, school or volunteering; we just want to make sure they don’t go back too early or quickly, when they might not be ready. There needs to be a balance between activity and rest after someone has a stroke because there is a lot of consolidation of learning and healing that happens at rest. But even though they’re not working, it’s important for people to engage in meaningful occupations. Hobbies or social activities give them that feeling that they’re being productive, and it’s also therapeutic because it promotes further stroke recovery. So I asked Marianne if there was a hobby she wanted to try, and she decided to try sculpting. Afterward, she gave me the amazing sculpture she made. It’s sitting in our office at work. It means a lot to know I’ve had this positive impact on Marianne’s life.

MARIANNE: It’s tempting, when you have a stroke, to say, “I can’t do this.” With the sculpting class, I didn’t know if my fingers would work properly, but I was sitting across from the live model and we had this smooth clay. I could do it. It was so therapeutic and freeing, because I wasn’t evaluating myself based on what I was pursuing as a career. I’m not a professional sculptor.

I’m also working on a play, which is about four people recovering from a stroke. I’m hoping to turn it into a musical. One of the characters is training to be a surgeon, but then she has a stroke and her hands no longer work the same. Her fine motor skills are affected. Over time, she realizes she may not be able to become a surgeon, but she could be a neurologist. I’m calling her Aleksandra.

a world-class regional stroke centre with a leading acute stroke team. Nurses and clinicians from radiology, anesthesiology and neurosurgery have to be ready to work together, fast. “We pride ourselves on a team-based approach to brain health care,” says Dr. Patrick Nicholson, a neuroradiologist at the KBI. “We train fellows from all over the world, so they go back home and hopefully help improve their systems of care locally.”

With treatments now available for more stroke patients, even for those who may have to fly to an advanced stroke centre, it’s that much more important to educate the public about strokes. Explains Dr. Timo Krings, a neuroradiologist and scientist at the KBI, and the David Braley and Nancy Gordon Chair in Interventional Neuroradiology. “While the majority of our population knows what the signs of a heart attack are, very few know the symptoms of a ‘brain attack’ or stroke and may thus not receive timely treatment,” notes Dr. Krings. “So this is one area where we can focus future research and education.”

Thanks to today’s neuro-interventional radiology procedures, someone can go back to their life after a major stroke, whereas just 10 years ago, they may have needed 24/7 care, explains Dr. Agid. “From being able to regain their vision or speech, or even walk again, we can now help many more stroke patients go back to a normal life,” she says. “There is no better feeling.”
DR. GELAREH ZADEH is a pioneer in the field of brain cancer research and neurosurgery.

Laser focus

A state-of-the-art brain disorder-fighting tool could make complex brain surgery a day procedure and save many more lives. BY CLAIRE GAGNÉ
sized probe through the skull. Once the probe is inside the brain, a laser heats the diseased tissue and liquefies it, allowing it to be removed with a suction. The patient lies in an MRI machine throughout the operation so surgeons can image their brain in real time. The true game-changer? The LITT can access previously inoperable tumours and lesions in patients with epilepsy, as well as brain cancer. “We used to just manage these hard-to-access tumours medically and symptomatically,” says Dr. Zadeh. “Now we can get rid of them.”

Decades of innovation

Dr. Zadeh sought out this technology – the KBI is one of two centres in the country that can do this procedure – because it’s critical to her that the KBI remain at the forefront of neuro-oncology. Nearly 20 years ago, the KBI began using Gamma Knife, which, at the time, was a groundbreaking technology that continues to save patient lives today. It works by sending focused beams of radiation to precise areas of the brain.

While Gamma Knife is still a critical tool, LITT allows Dr. Zadeh and her colleagues to get at even more complicated cancers. “This is an incredibly innovative technology. I wanted to acquire it so we could continue to stay at the cutting edge,” she says, adding that the expertise of two of her colleagues, Dr. Suneil Kalia, who has a functional neurosurgery background, and Dr. Paul Kongkham, who has extensive oncological knowledge, has been instrumental in getting the technology up and running safely.

Dr. Zadeh is also pushing brain cancer boundaries in her lab. Together with scientist and collaborator Dr. Daniel De Carvalho, she has developed a groundbreaking blood test that can detect not only whether someone has brain cancer but the specific type of brain tumour, too. This has tremendous implications for patients. “It’s potentially a replacement for the need to do a biopsy diagnosis,” says Dr. Zadeh. “Ultimately, we hope it could be used as a tool for early detection of brain cancer and to assess response to therapy and detect recurrence early.” Dr. Zadeh and her team published a paper on the blood test in May 2020 and are now conducting trials to see if it can become a clinical-grade test.

Dr. Zadeh says that in addition to Ontarians, she and her team would welcome an opportunity to care for out-of-province patients using the LITT technology and will work with patients and their healthcare teams to make this happen. “It’s a technology at the intersection of neuroscience and cancer,” she says. “It gives us the advantage of bringing the two worlds together.”
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