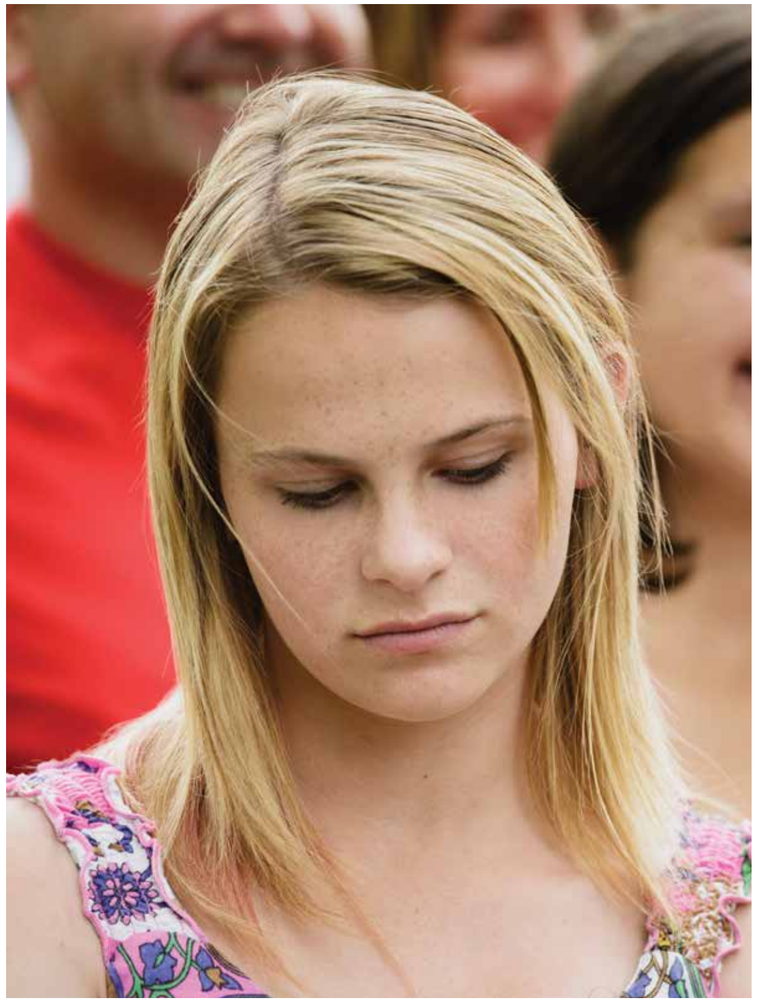
UNIVERSITY OF CALGARY

Hotchkiss Brain Institute

2014: Celebrating 10 years of excellence in brain and mental health research and education

HOTCHKISS BRAIN INSTITUTE
Improving brain and mental health in your community for 10 years

hbi.ucalgary.ca



Almost 20 per cent of Canadian youth, approximately 1.5 million individuals, suffer from a diagnosable psychiatric disorder.
- Canadian Mental Health Association, Alberta Division

Learn about research in our Brain & Behaviour priority on page 9.

Brain injury is the leading cause of death and disability for Canadians under 35 years of age. There are more than 10,000 new cases of brain injury annually in Alberta.
- Brain Injury Association of Alberta

Learn about research in our Neural Injury, Repair & Rehabilitation priority on page 13.

There are 40,000 people with dementia in Alberta, 17 per cent are diagnosed under the age of 65 years, which is the highest prevalence of early-onset dementia in Canada.
- Alzheimer Society of Alberta and Northwest Territories

Learn about research in our Healthy Brain Aging priority on page 17.

2004 — The Hotchkiss family provided the initial lead gift of $10M to establish the Hotchkiss Brain Institute at the University of Calgary. This remarkable gift set the institute on a trajectory to become an internationally recognized centre of excellence in neurological and mental health research and education.

2007 — V. Wee Yong, PhD, and Dr. Luanne Metz led a Multiple Sclerosis Society of Canada-funded study into a common acne medication with the potential to delay the progress of multiple sclerosis (MS). With outstanding support from community leaders, such as Mr. Jay Westman and Mr. Hank Swartout, they continue to create new medicines for repairing damage and recovering function in people with progressive MS.

2008 — Samuel Weiss, PhD, earned a Gairdner International Award for his discovery of neural stem cells in the brains of adult mammals and their importance in nerve cell regeneration. Gairdner Awards recognize the world's most accomplished biomedical scientists who have made original contributions to medicine resulting in increased understanding of human biology and disease.

2011 — Community members, led by Mr. John Lamacraft, spearheaded the launch of the Rebecca Hotchkiss International Scholar Exchange (RHISE) program. RHISE has driven the HBI's international research and education agenda by promoting interactions with visiting scholars from abroad, while also supporting HBI members and trainees to exchange ideas and learn at other world-renowned institutions of neuroscience.

2012 — Concussion and brain injury research spearheaded by Carolyn Emery, PhD, and Dr. Willem Meeuwisse influenced changes in public policy. Their findings contributed to a landmark Hockey Canada ban on body checking in peewee hockey that will prevent an estimated 3,500 concussions per year across Canada.

2013 — Bruce Pike, PhD, was appointed as the new Campus Alberta Innovates Program Chair in Healthy Brain Aging. His human brain-imaging research has implications for the study of normal brain development and the diagnosis and treatment of diseases such as MS, stroke, depression and dementia. Pike is leading the recruitment of brain imaging experts and the development of a neurotechnologies platform at the HBI.

2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014

Hotchkiss Brain Institute

Top 10 Highlights

World-class research and education has been improving brain and mental health in your community for 10 years.

2008 — Dr. Garnette Sutherland made history using the neuroArm, an image-guided neurosurgical robot, to operate on a human patient for the first time to remove a brain tumour. This surgical robotic system has revolutionized neurosurgery and other branches of operative medicine.

2010 — Dr. Sean Dukelow helped develop a robotic stroke assessment and therapy delivery tool, the KINARM: Kinesiologic Instrument for Normal and Altered Reaching Movements. The technology, recently adapted for use with patients suffering from concussion, enables improved rehabilitation outcomes after stroke and brain injury.

2012 — The Mathison Centre for Mental Health Research & Education was founded by a $10M investment from Mr. Ronald P. Mathison. The centre supports research into the early identification, prevention and treatment of mental illness with a special emphasis on youth mental health, offering new hope to families in Alberta and beyond.

2014 — New Healthy Brain Aging Laboratories are under construction to support collaborative research in the areas of stroke, dementia and movement disorders. Researchers studying cutting-edge brain imaging, neural stimulation and clinical research approaches will work together in this innovative space, including Oury Monchi, PhD, recently named as the first holder of the Tourmaline Oil Chair in Parkinson's Disease.

Report to the Community

Table of contents

Message from the President

This year marks the Hotchkiss Brain Institute's 10th anniversary — an exciting milestone for the institute, the Cumming School of Medicine and the University of Calgary. The past decade has been defined by true distinction in neurological and mental health research and the translation of these discoveries into innovative health care solutions that directly benefit Canadians and people around the world.

The University of Calgary has benefitted from the ongoing generosity of the Hotchkiss family and new support for brain and mental health research through the naming of the Cumming School of Medicine. With the continued support from our surrounding community, as well as with the able leadership of Samuel Weiss, PhD, we anticipate not only another decade, but generations of research breakthroughs at the HBI.

As Canada's leading next-generation university, we believe that innovation in research, clinical care and education are central to our success and we are proud to be home to this top-calibre research institute that exemplifies these qualities across its activities and endeavours. With more than 150 faculty members across our institution researching Brain and Mental Health, one of the University of Calgary's strategic research themes, the HBI is well situated to accelerate research and translate this knowledge to have great impact throughout the community.

I would like to offer my sincere thanks to the students, faculty, researchers and staff, our alumni and our community of support, which has built this centre of research excellence here at the University of Calgary. Together we are building a better future and laying the groundwork for another extremely promising decade ahead.

Sincerely,

Elizabeth Cannon
President and Vice-Chancellor
University of Calgary

Message from the Dean

It gives me great pleasure to celebrate the 10th anniversary of the Cumming School of Medicine's Hotchkiss Brain Institute. Over the past 10 years, the HBI has been a leading force in the creation and growth of an internationally recognized hub for brain and mental health research and education at the University of Calgary.

The HBI has helped to bring together and build our strengths in basic, translational and clinical research, from the study of concussion to mental illness; neuroscience to brain cancer.

Researchers at the HBI have revolutionized neurosurgery and discovered adult neural stem cells; they work at the forefront of multiple sclerosis research and have shown that a drug can protect the brain from stroke damage.

Our institutes were created to inspire collaboration; to promote working together and crossing disciplinary boundaries. I am tremendously proud of the passion for teamwork that underpins all of our institutes at the Cumming School of Medicine. When people, ideas, infrastructure and resources come together, we create the best possible environment for innovation to spark and thrive, and innovative medical research always leads to better health care.

Congratulations to the HBI faculty, staff, students and trainees who contribute daily to the maintenance and ongoing evolution of that passion. The success of the HBI yesterday, today and tomorrow is a reflection of your incredible collective commitment to creating the future of health.

Happy anniversary!

Jon Meddings, MD
Dean, Cumming School of Medicine

Message from the Director

More than 10 years ago, then Dean of Medicine, Dr. Grant Gall, asked me to create a concept for a brain institute in Calgary — to bring together scientific and medical minds and better inform health care delivery for diseases and injury of the brain and spinal cord.

It was an ambitious proposal that required equally ambitious support. Three critical thought leaders and creative supporters — Dr. Alastair Buchan, Mr. Jack Davis and Dr. Chen Fong — arranged for me to take the proposal for community endorsement to one of Calgary's most prominent citizens.

When I first met Harley Hotchkiss in the fall of 2003, he greeted me with a warm smile and a strong handshake. Though our conversation quickly turned to hockey, it didn't take long to realize that we also had a common vision when it came to our community — to enable high-quality medical research in a collaborative environment for the ultimate goal of improved brain and mental health.

And so, in October 2004, the Hotchkiss Brain Institute was created — a direct result of the Hotchkiss family's personal and financial commitments.

The past decade has been extraordinary and I have no doubt Harley would be proud. We started by organizing ourselves to be greater than the sum of our parts — bringing together the three research groups and five academic departments at the time to form connections between neurological health and mental health, research and education, basic (foundational) science and clinical science.

After the first five years, with those connections in place, we turned our attention to effectively translating the best foundational science into our clinical programs, such that knowledge could be directly applied to developing diagnostics and therapeutics. We focused on four major programs: multiple sclerosis; spinal cord and nerve injury; stroke and vascular dementia; and depression and psychosis.

Now, just 10 years from where it all began, we are a thriving organization comprised of 750 faculty members, trainees and staff, all of whom are proud to be part of the HBI and make outstanding contributions every day. The institute has become a top-ranked, nationally recognized centre of excellence in brain and mental health research and education, with an increasing international reach.

Looking forward, we are now strategically charting our course for the next 10 years and beyond and increasing our capacity to conduct groundbreaking research for the benefit of our community.

We are developing our strengths using a formula:

NeuroTeams + NeuroTechnologies = NeuroDiscoveries

Essentially what this means is that dedicated, multi-disciplinary teams (NeuroTeams) from across the University of Calgary, combined with cutting-edge, innovative technologies (NeuroTechnologies), such as brain imaging and brain stimulation, will result in important brain and mental health discoveries (NeuroDiscoveries).

We are focusing on three priority areas, representing the most prevalent problems that our society faces throughout every stage of life: Brain & Behaviour; Neural Injury, Repair & Rehabilitation; and Healthy Brain Aging.

By building collaborative teams of the best researchers that have access to leading-edge infrastructure and technologies, we will further our understanding of the brain and improve brain function in ways that will be truly transformative.

I am excited to share with you a glimpse of our past, present and future throughout this report. I think it's fair to say that for the HBI and Brain and Mental Health at the University of Calgary, the best is yet to come!

I would like to take this opportunity to thank the Hotchkiss family for their ongoing involvement in everything we do. While Harley will be forever and dearly missed, his values continue to guide the HBI and we are grateful for the continued and steadfast support of his entire family.

We have the privilege of operating within an enriched environment at the innovative Cumming School of Medicine and receive incredible support from the University of Calgary — a young institution, but one with tremendous ambition. Thanks also to all of the department heads, associate deans and deans in the Cumming School of Medicine and the senior leaders of the University of Calgary — past and present — who have been outstanding colleagues and inspired leaders in the HBI's trajectory.

A very special thank you to my close friend and colleague, Keith Sharkey, PhD, Deputy Director of the HBI, a remarkable and critical partner for success over the past five years. Keith's selfless efforts have helped position the HBI for a continuing run of great achievements in the future.

As importantly, thanks to all of you, our community members, partners and stakeholders. We are fortunate to have extraordinary support, particularly from our local community and it is this generosity that allows us to continue on the path of creative, relevant and impactful discovery.

I hope you enjoy this special 10th anniversary *Report to the Community* and look forward to what we are able to achieve together in the next 10 years and beyond!

Samuel Weiss, PhD, FRSC, FCAHS
Professor and Director
Hotchkiss Brain Institute

A labour of love for the Hotchkiss family

The Hotchkiss family pictured at a recent family gathering. Standing (from left): Richard and Paul. Seated (from left): Jeff, Brenda, Rebecca and John.

Although it's been a decade since the official launch of the Hotchkiss Brain Institute, Rebecca Hotchkiss' heart still beats a little faster every time she sees the name.

The widow of the late Harley Hotchkiss shares her pride with family members who appreciate the research, leadership and innovation at the HBI and their family's role in bringing it to life. The institute was enabled by a foundational gift from the Hotchkiss family, launched in October 2004 under the leadership of Samuel Weiss, PhD.

The institute has become far more than one of the family's many community investments. It has become a member of the family, reflecting the compassion, integrity and values synonymous with the Hotchkiss name.

"My father believed that research into brain and mental health would help people," explains Brenda Mackie, who has led the family's involvement with the HBI since Harley passed away in 2011. "He saw a need and was compelled by a responsibility to give, to better the community, whether that was through money or time." He did both.

"Harley also believed that when you support a cause, you get involved," Rebecca adds. "He was hands-on."

This philosophy continues in the family, with several members currently sitting on the institute's advisory boards and committees.

"When something has your family name, you take ownership," Brenda says simply. "The Hotchkiss name is held in high esteem and it's important to us that we carry on that legacy. We want to ensure that people know about my dad, what his name stands for and who he was."

Brenda chairs the institute's Strategic Advisory Board. She is also chair of the Fundraising and Stewardship Committee, with her brothers Jeff and Richard serving as committee members. Rebecca and Brenda are both members of the Community and Partners Advisory Committee alongside Jeff's wife, Sheryl.

Many of the Hotchkiss family values are woven into the DNA of the institute.

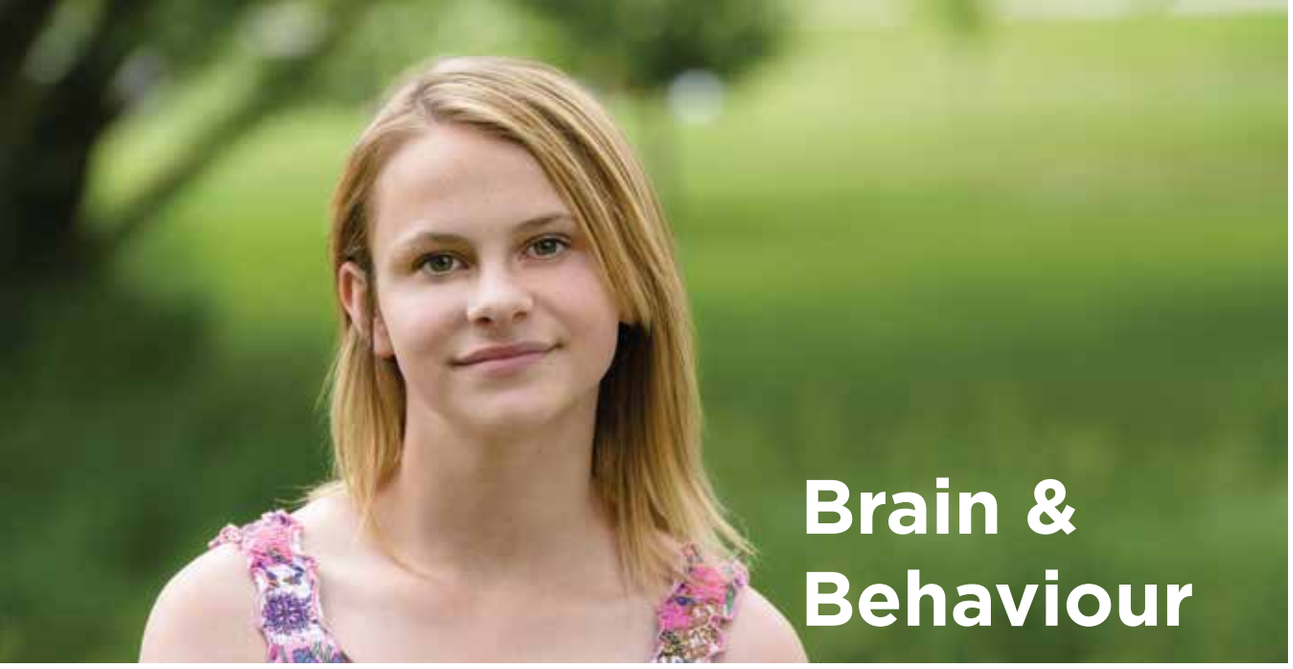
"Dad loved research, thrived on collaboration, was always interested in what others had to say and liked that people from different fields worked together at the HBI," Brenda says. "He enjoyed bringing people together to solve a problem, to make a difference in people's lives."

The family has seen first-hand the impact the institute is having in the community. An HBI-supported clinical trial is helping to improve recovery and save lives of stroke patients across Canada — including the life of a family friend's daughter.

"Research at the HBI is having a real impact. Talented, young investigators from around the world are eager to come here and the institute is on an upward trajectory. It's both rewarding and humbling to be part of it," Brenda says. "We're thankful we have the opportunity to be so involved and see all this happen."

The Hotchkiss family is confident that the institute will continue to be an instrumental force for improved brain and mental health in the community. Inspired by hope that further discoveries will lead to more insights and advanced treatments, the family continues to champion research and education at the HBI that will help improve lives for decades to come.

"Harley wouldn't be surprised by all that the HBI has achieved in its first 10 years," Rebecca says. "He'd be proud that he helped bring it all together and excited to see what happens next."



Brain & Behaviour

Every thought, every feeling and every movement is governed by the dialogue that occurs between the cells in our brain. This dialogue is remarkably resilient and can be modified by external factors and personal experiences.

For some people, abnormal connections between cells in the brain can lead to problems with how the brain processes information, ultimately affecting a person's behaviour, mood, perception or thinking.

Researchers in the Brain & Behaviour priority are applying collaborative approaches and cutting-edge technology to advance our understanding of the cellular communication in the brain and how it influences behaviour. This research is guiding new treatments for existing conditions as well as developing important early-stage interventions to prevent the progression of disease, particularly in young people.

Brain & Behaviour research today at the HBI:

The Mathison Centre for Mental Health Research & Education

Launched in 2012, The Mathison Centre for Mental Health Research & Education was made possible by a $10 million investment from Mr. Ronald P. Mathison, President and CEO of Matco Investments Ltd.

THE MATHISON CENTRE
for MENTAL HEALTH RESEARCH & EDUCATION

The Mathison Centre aims to generate knowledge to improve our understanding of the brain mechanisms, risk factors and treatments of mental disorders, with special emphasis on youth populations.

Created by the HBI and the Department of Psychiatry, The Mathison Centre partners with the Cumming School of Medicine and other faculties at the University of Calgary, supporting 40 members with expertise in brain imaging and mental health research. These researchers and clinicians are attracting competitive funding from national organizations such as Brain Canada and the Canadian Institutes of Health Research to better inform mental health care strategies in our community and offer new hope to families in Calgary, throughout Alberta and the world.

mathison.ucalgary.ca

Youth mental health

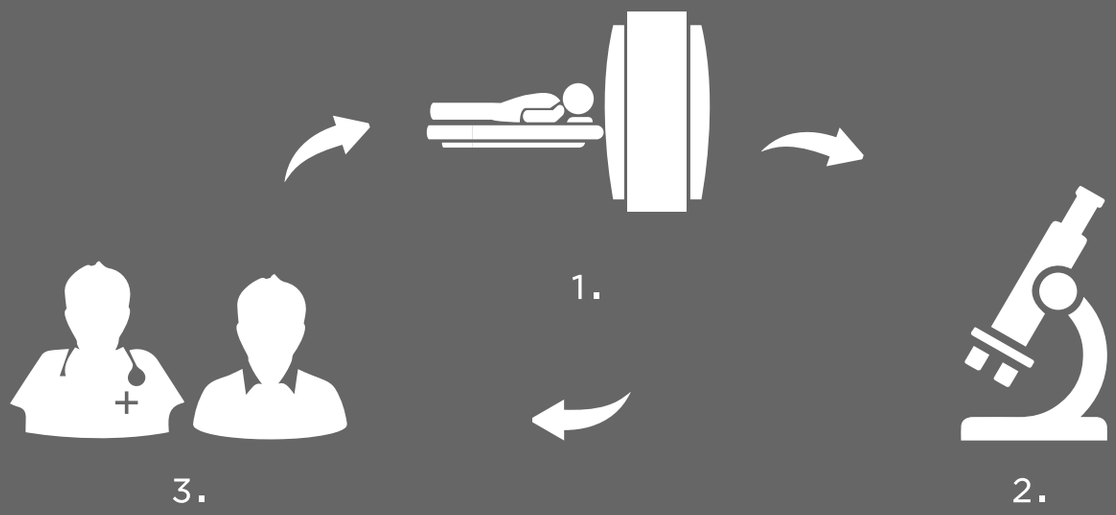
Most mental disorders begin in adolescence, however there are many gaps in our understanding of youth mental health. Jean Addington, PhD, the Novartis Chair in Schizophrenia Research, focuses on understanding risk factors and identifying predictors that may impede the development of serious mental illnesses. Working with young adults and adolescents as young as 13, she seeks to determine whether symptoms can be predicted and treated prior to the development of serious mental illness.

Behavioural impacts of stress

How the brain reacts and adapts to stress, through changes to cells and circuits within the brain, remains for the most part, a mystery. Jaideep Bains, PhD, is working to understand how stressful situations can lead to long-term changes in how individual brain cells and brain circuitry function. Bains' current work uses advanced technologies such as optogenetics — genetically engineered, light-based proteins used to visualize, activate or inactivate the brain circuits that control behaviour in animal models — to establish links between early-life stress and changes to neural circuits that are related to the emergence of behavioural changes later in life, such as anxiety and depression.

The future of Brain & Behaviour research at the HBI:

The future of Brain & Behaviour research at the HBI lies in the integration of science and health, achieved through the seamless collaboration of the laboratory and clinic. This ensures a continuous cycle of fully integrated research that will ultimately guide improved prediction, prevention and early intervention strategies to treat neurological and mental health disorders.



Interdisciplinary teams will use data from clinical populations, such as MRI images from adolescents with stress and anxiety disorders (1), to develop and test targets and therapies in the laboratory (2), which will then be used to develop clinical trials in human patients (3). Data from clinical studies is then used to further refine therapies in the laboratory.

Stephanie Borgland, PhD, (right) is pictured with Shuai Liu, PhD, a postdoctoral fellow in her laboratory investigating learning cues that predict food reward. The study is funded by the Canadian Institutes of Health Research.

Understanding the circuitry of compulsive overeating

We've all asked ourselves the same question: Why? Why did I eat that entire sundae? Why did I open that bag of chips? Why did I order the double burger?

For most of us, it's a rhetorical query that comes with an inkling of hope that willpower prevails the next time temptation comes knocking. But for the 2014 Canadian Association for Neuroscience Young Investigator Award winner, it's a scientific journey aimed at settling an ever-present quandary in North American society.

"People eat when they're full. People take abusive drugs when they're completely aware of how harmful they are. There are multiple reasons why," says Stephanie Borgland, PhD. "My research is essentially about understanding why we do things even though we don't really want to do them."

Borgland recently joined the University of Calgary as an assistant professor in the Cumming School of Medicine's Department of Physiology and Pharmacology. Her work is helping the HBI focus on one of it's research priority areas: Brain & Behaviour.

Studying what's happening in the human brain is no simple task. The brain is the most complex organ in the human body, constantly changing with experience, environment and time. "It's like a giant switchboard with a tiny operator rearranging circuits depending on the nature of each call," explains Borgland. Her research studies two of these circuits: one that helps us learn cues that predict a reward and another that makes it hard for us to resist the desire to get that reward.

Take a chocolate bar as an example (or chips, if salt is your nemesis). The first time you eat one, your brain's dopamine neurons fire off to let you know this is a happy thing to be eating.

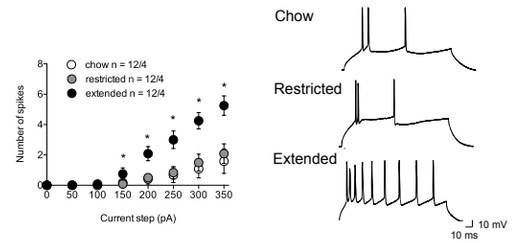
"Over time, even the wrapper will give you a reward response because you know what's inside," says Borgland. The challenge comes in resisting the temptation to seek that reward. That's the job of the brain's orbital frontal cortex. It's where we assess the value of our actions, like whether eating a chocolate bar is really a wise idea.

"I hope that my research will lead to greater public understanding of the mechanisms of disease, ultimately to have a positive influence on people's behaviour in relation to the harmful effects of indulgence and overeating."

"People with damage to this area of the brain may still recognize that they shouldn't eat the candy," says Borgland, "but they're unable to process the information in a way that helps them make the right choice." Some of it boils down to pure habit. We like the taste of the food so we keep eating it despite being full. Borgland and her collaborators are attempting to find out what's actually happening in the brain when we make these choices.

"No one really knows the specifics of how these neurons are communicating and what circuit is involved," she says. "We're trying to understand the changes that take place when the desire for that reward response starts to take control."

By understanding how the brain changes towards these behaviours, Borgland will be able to experiment with strategies to help change it back. To achieve this, she is forming strong collaborations with other HBI members across various studies related to obesity and addiction.



Rats with extended access to a cafeteria diet have increased firing of pyramidal neurons in the orbitofrontal cortex (a region important for cognitive processing and decision-making). This increased firing activity may underlie the compulsive feeding behaviour observed in these rats.

One project with Frank MacMaster, PhD, a member of the HBI and the Alberta Children's Hospital Research Institute, is looking at how a hormone regulates a neurotransmitter in the brain that may have a role in obesity in children.

The neurotransmitter, called glutamate, has an important function in the brain and notably in the hippocampus — an area that is responsible for learning and memory. Through brain imaging studies on a group of obese children, MacMaster has observed increased glutamate in the hippocampus.

Leptin is a hormone released by fat tissue that has been found in higher levels in obese individuals.

"Therefore, we hypothesize that obese individuals have abnormal glutamate signaling in their brains due to the presence of higher leptin levels," explains Borgland. "We believe this may influence eating behaviours that lead to obesity."

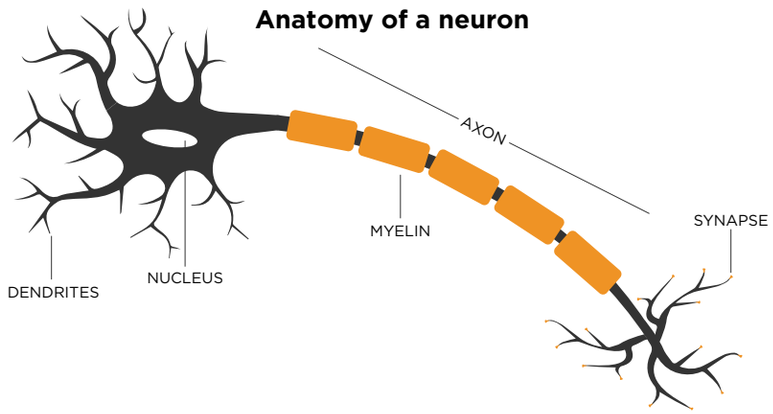
Understanding the mechanisms within the brain that lead to obesity is an important first step towards developing potential treatments.

In time, Borgland hopes her research will enable people to win the eternal battle of mind over matter, to influence behaviours and adopt a healthier lifestyle.

Neural Injury, Repair & Rehabilitation

Neurons and glia are the building blocks of the nervous system. Injuries to neuronal and glial cells are devastating and often lead to lifelong disability. Nervous system injuries can be a consequence of accident or illness and therefore they are difficult to predict or prevent.

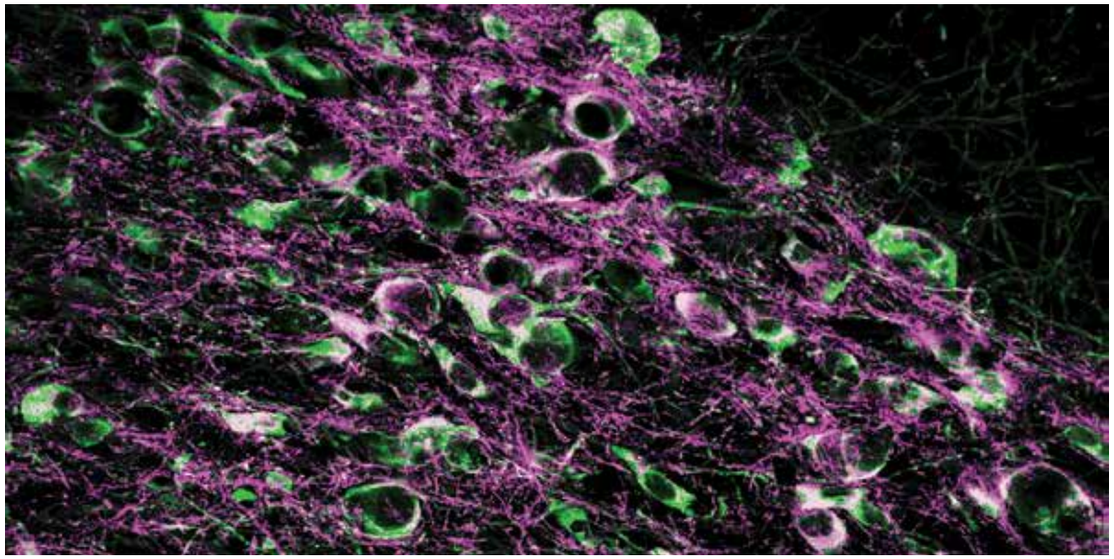
Researchers in the HBI's Neural Injury, Repair & Rehabilitation priority are searching for new ways to treat damaged neurons and glia. Using advanced technologies such as sophisticated imaging, robotics and biomedical techniques, our research teams are translating their findings into effective therapies to improve the lives of nerve-injured patients.



Neural Injury, Repair & Rehabilitation research today at the HBI:

Regeneration Unit in Neurobiology

Developing safe and effective therapies for neural injuries requires the ability to take investigations from cells in a petri dish to patients in a clinic. Researchers at an HBI preclinical facility that opened in 2010 have that ability. The Regeneration Unit in Neurobiology (RUN) was created through funding from the HBI, the University of Calgary, Western Economic Diversification, Canada Foundation for Innovation, Alberta Innovation and Advanced Education, and Integra LifeSciences. This cutting-edge facility provides resources and innovative equipment to develop new therapies and biomedical engineering solutions for reconnecting broken and damaged nerve fibres with an eye towards the development of new treatment approaches for people affected by neurological injury or disease.



Neurons in the motor network of mice stimulated by light-activated mechanisms. Photo credit: Whelan Lab.

The future of Neural Injury, Repair & Rehabilitation research at the HBI:

Neurorehabilitation

Dr. Sean Dukelow (left) and the robotic assessment and therapy delivery tool: KINARM (Kinesiologic Instrument for Normal and Altered Reaching Movements). The technology, initially developed for stroke patients, was recently adapted for use with patients suffering traumatic brain injury and concussion. The KINARM helps Dukelow study the impact strokes and brain injuries have on people to improve rehabilitation outcomes for patients.

Once thought to be completely irreversible, we now know the brain and spinal cord possess the ability to change and reorganize following injury. This reorganization, or neuroplasticity, has opened the door to innovative research aimed at maximizing recovery and quality of life — a process referred to as neurorehabilitation.

Researchers at the HBI, such as clinician-scientist Dr. Sean Dukelow, are exploring the use of robotics, biomarkers, brain imaging and brain stimulation to enhance the therapeutic power of current rehabilitation strategies.

"The HBI has a critical mass of investigators interested in advancing rehabilitation and recovery from neural injury," says Dukelow. "We know that neurorehabilitation works, so now the focus is on developing new drugs, brain stimulation and other techniques to improve our treatments even further."

Having clinicians like Dukelow located on the same campus as basic scientists is giving the HBI an edge when it comes to quickly translating discoveries into neurorehabilitation therapies. For example, in the University of Calgary Acute Neurorehabilitation (UCAN) program, a new initiative led by Patrick Whelan, PhD, basic scientists and clinicians will work together to investigate ways to quickly mobilize the plasticity of the nervous system after injury. In addition to advanced robotics, imaging and stimulation technologies, researchers are using biomarkers in the blood to predict recovery from neural injuries.

"The HBI is becoming one of the few places in the world to take a truly collaborative approach to advancing neurorehabilitation," says Dukelow. "When the physicians providing care and the scientists developing therapies have the ability to work together, the continuous feedback loop that creates ensures the most efficient translation of discovery, ultimately improving clinical care."

Shalina Ousman, PhD, (right) is pictured in her laboratory with Vahid Hoghooghi, PharmD, a PhD student funded by a Multiple Sclerosis Society of Canada doctoral studentship.

Mysterious molecule surprises MS researchers

In the world of neuroscience, there are few diseases as enigmatic as multiple sclerosis (MS).

"It seems that almost every patient has a different disease," says Shalina Ousman, PhD. Ousman is an assistant professor at the University of Calgary's Department of Clinical Neurosciences in the Cumming School of Medicine. Her work on MS is helping the HBI break new ground in one of its research priority areas: Neural Injury, Repair & Rehabilitation.

"We don't yet know how MS initiates," she explains. Finding the cause is akin to the holy grail for MS researchers, but the disease is difficult to study. "By the time you diagnose it, MS is probably a couple of decades past whatever was the initiating factor."

Hypotheses abound. It could be environmental or genetic or likely both. It could be immune-related or an issue with the nervous system. For Ousman, the question is how the body deals with the disease once it starts.

"Whenever we encounter injury, like a bruise or a cut, our bodies mount a normal healing mechanism," she says. "That must also happen in MS."

Ousman is focusing her research on identifying that healing response to the disease. Her theory is, if we understand what's trying — but failing — to kill the disease, we might be able to boost its success.

Her search narrowed in on a molecule called Cystatin C, a needle in a haystack of potential clues. Some literature suggests it helps keep neurons alive. Other research suggests it's responsible for neuron death. Ousman decided to find out for herself. The results came as a complete surprise — a researcher's dream come true.

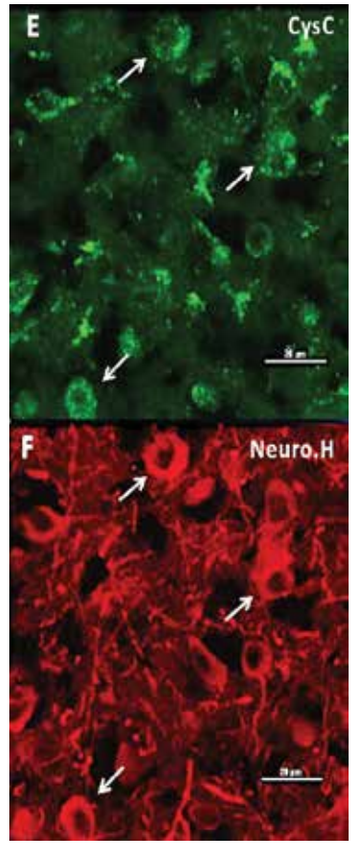
"Being a discoverer you have no idea what's going to happen every day."

"We went in thinking this was going to be a protective molecule, in that if you remove it, the disease will get worse," she says. "It was the total opposite! The disease improved without it."

The other surprise was the gender inequity. Removing the Cystatin C only demonstrated improvements in the clinical symptoms of the autoimmune disease for females. There was no change for the males. This was a particularly relevant discovery because more females develop MS than males.

"We ended up with two projects," she says, clearly excited by the road ahead. "Not only what is the role of Cystatin C, but also what is its role in the gender difference? Finding out if it's playing a role in the immune system, the nervous system or both is where all the nitpicky cell biology experiments occur."

Ousman's research into the role of Cystatin C in MS is enabled by a Canadian Institutes of Health Research operating grant, with additional experiments also supported by the Multiple Sclerosis Society of Canada. To begin to understand the fundamental, biological processes in these experiments, her laboratory uses an animal model of MS as well as cells from mice. Based on research obtained through these models, the influence of the molecule can then be evaluated in human immune cells.



The Cystatin C molecule is expressed by neurons. These cells (F) are co-localized with Cystatin C positive profiles (E) in the spinal cord of an animal model of MS.

Being at the HBI is giving Ousman a unique opportunity to work on a human study with Dr. Luanne Metz, co-director of the institute's MS program.

"We're setting up a collaboration where we can compare blood samples from MS patients and controls," says Ousman. "We're going to isolate the immune cells, then add Cystatin C to see if it changes their activation status." This would confirm that the effects, initially discovered in animal cells, also have relevance to the disease in human cells.

Ousman is optimistic that solving the Cystatin C mystery will provide some much needed clues to help lead new MS research down the right path.

Healthy Brain Aging

The life expectancy of Canadians has risen significantly in the past century. The average Canadian now faces an increased risk of experiencing health issues associated with degenerating nervous and vascular systems.

These diseases and conditions have familiar names — Parkinson's, dementia and stroke. Researchers in the Healthy Brain Aging priority are working to better understand the interplay between aging and the increased risk of dysfunction in the nervous and vascular systems. They aim to identify new ways to detect and prevent diseases and conditions associated with the aging brain, as well as to improve treatments and outcomes for individuals already dealing with age-related brain health challenges.

Healthy Brain Aging research today at the HBI:

Collaborative, interdisciplinary teams — basic scientists working working hand-in-hand with clinicians — are making discoveries that are translated into innovative, life-saving treatments.

Calgary Stroke Program

Donna Sharman is pictured with HBI members, Drs. Michael Hill (centre) and Andrew Demchuk (right), who recently received a $5 million grant from Alberta Innovates - Health Solutions to continue their innovative stroke research.

The Calgary Stroke Program provides quality acute, rehabilitative and preventative care to people with stroke and their families – like Donna Sharman, who in 2013 suffered an acute ischemic stroke and was enrolled in an HBI-supported clinical trial that may have saved her life. Collaborators in this study hypothesize that inserting a small stent-like device in people who have had this type of stroke (when a blood clot that blocks an artery to the brain) is more effective than routine medical care. For Donna, participating in this research study made all the difference.

World-class Parkinson's Disease research supported by the community

Introducing Oury Monchi, PhD, the first holder of the Tourmaline Oil Chair in Parkinson's Disease.

Monchi is a pioneer in using brain imaging techniques to study the origins and evolution of cognitive deficits in Parkinson's, with the ultimate goal of the early prediction of dementia in the disease. He will work with scientists and clinicians conducting research related to healthy brain aging in the areas of stroke, dementia and movement disorders.

Nearly 100,000 people in Canada live with Parkinson's, a degenerative disorder of the central nervous system for which there is no cure. Thanks to the vision and generosity of the management and staff at Tourmaline Oil Corporation and Peters & Co. Limited, Monchi and his team have an unparalleled opportunity to conduct patient-focused, groundbreaking research on the disease. They are testing treatments that help improve — or slow down the evolution of — cognitive deficits in Parkinson's, demonstrating a real impact for people living with this disease.

Oury Monchi, PhD, is pictured with Mr. Michael Rose (left), President of Tourmaline Oil Corporation and Mr. Christopher Potter (right), President of Peters & Co. Limited.

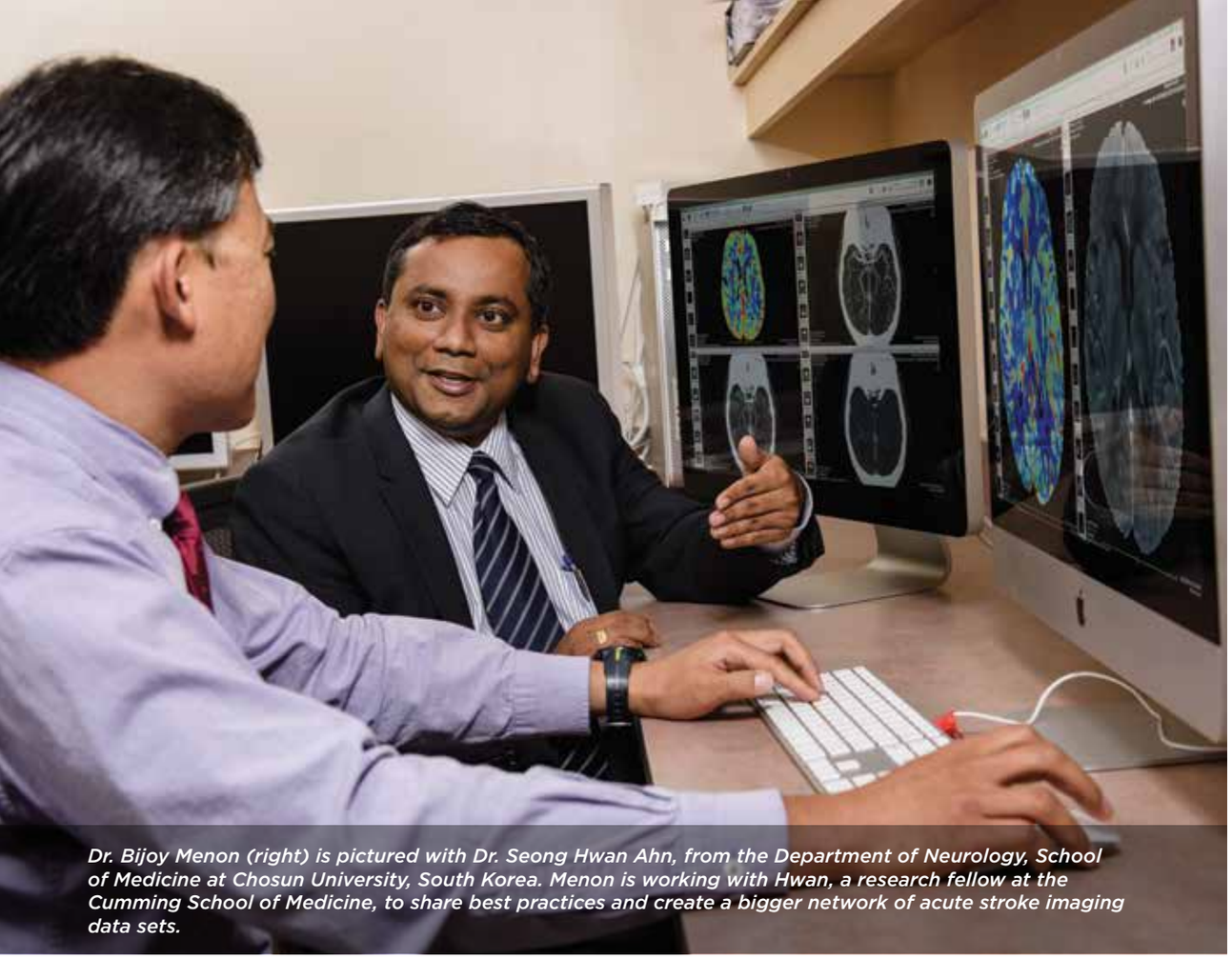
The future of Healthy Brain Aging research at the HBI:

Healthy Brain Aging Laboratories

Scheduled to open in early 2015, the HBI's Healthy Brain Aging Laboratories are a new 111m^2 facility that will serve as the hub for research associated with the aging brain in the Cumming School of Medicine at the University of Calgary.

This state-of-the-art facility, supported by the Ronald and Irene Ward Foundation, is designed to maximize interactions between researchers to accelerate discovery and dramatically transform our approach to the prevention and care of age-related brain dysfunction.

The collaborative space will bring together psychiatrists, brain imaging experts, population health researchers, molecular scientists, clinical investigators and trainees who are studying healthy brain aging at every level. Research will span from the cellular and molecular basis of blood flow in the brain using sophisticated microscopy tools and technologies, to enrolling the local community in clinical studies examining the relationship between vascular risk factors and cognitive decline.



Dr. Bijoy Menon (right) is pictured with Dr. Seong Hwan Ahn, from the Department of Neurology, School of Medicine at Chosun University, South Korea. Menon is working with Hwan, a research fellow at the Cumming School of Medicine, to share best practices and create a bigger network of acute stroke imaging data sets.

Collateral status holds the key to stroke recovery

When you walk into Dr. Bijoy Menon's office, one thing becomes abundantly clear: this man's mind never stops. It probably hasn't since he got into medical school at the ripe old age of 16.

"I didn't have a choice," he says with a laugh. "My mom made me do it!"

There's an easel by the window with what looks like the birth of a scientific theory scrawled down the page. A white board by the door has drawings of bisected blood vessels. Flowchart-adorned papers are tacked to a corkboard above his desk.

"There are many off-shoots to my research," says the stroke neurologist and assistant professor in the departments of clinical neurosciences and radiology, who was recently awarded the Heart and Stroke Professorship in Stroke Imaging.

His work is helping the HBI explore one of its research priorities: Healthy Brain Aging.

"I'm trying to identify why different people have different strokes," Menon says. His research aims to understand how an identical blood clot can result in varying severity and effects of a stroke from person to person. Physicians could then use this knowledge to customize treatment and ultimately improve outcomes for stroke patients.

To do that, Menon is focusing on the tiniest of blood vessels in the brain. Collaterals, as they're called, are the blood's detour route when a clot blocks one of the larger arteries.

"Sometimes you can't prevent the clot from happening, but if you have better collaterals your chance of recovery is greater than someone who has poor collaterals," he explains. People who have good collaterals will suffer less damage from a stroke because the blood can find another way to get to the brain. But not everyone has such a robust network of vascular side streets. For some people it's the highway, or no way.

"We're using brain imaging techniques to determine the best way to investigate collaterals," he says, "because we know they have such a high impact on a patient's outcome."

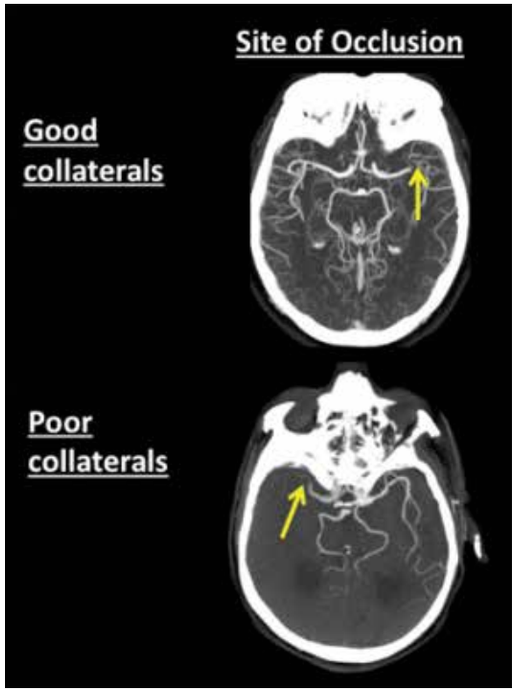
"In the future we may be able to use this new information to not only customize treatment for stroke patients, but also educate the public on the best ways to maintain and improve brain health."

Menon's current research is multi-pronged. First, he's trying to find the fastest and most accurate way to assess a patient's collaterals. Time is of the essence during an acute stroke so the tests have to be quick and precise. Accurate imaging will not only help doctors assess how well the patient will respond to treatment, it will also help Menon find the reasons behind unhealthy collaterals.

"It could be high uric acid, or the fact that you're taking a certain drug, or that you have hypertension," he says. "Those are modifiable factors in that we can do something to change them. There could also be genetic factors."

Menon believes that more minds work better than one. His imaging expertise is engaging colleagues here in Calgary, across Canada and around the world, collaborating on research and clinical trials that are testing new therapies and working to improve accessibility and speed of treatment for stroke patients.

Thanks to recent funding from the Canadian Institutes of Health Research, Menon is developing a new brain imaging procedure together with HBI colleague and interventional neuroradiologist, Dr. Mayank Goyal. With the aim to enhance standard of care and inform best practices in stroke treatment, their study seeks to perform a new technique called multi-phase CTA scanning on 600 patients from eight internationally-renowned stroke centres. "We already have 200 patients from our own centre and we're working with others in Canada, as well as Spain, Sweden, Italy, India and the Czech Republic," he says.



Multi-phase CTA scans of stroke patients (blockage indicated by the arrow) demonstrating examples of good collaterals (top) and poor collaterals (bottom).

The study will analyze the correlation between collateral quality and patient outcome to determine which stroke patients might benefit most from certain therapies. Their research will also collect demographic and lifestyle information from patients to help understand why some people seem to have better collaterals than others.

Menon's theory is that understanding what causes poor collaterals — whether it is genetics, ethnicity or lifestyle — will help him find ways to improve them. Doing that could improve outcomes and quality of life for thousands of stroke patients who may have otherwise had little chance for recovery.

Finding a new vision through education

Smriti Agrawal, PhD, is pictured at the Rockyview General Hospital in Calgary, AB, where she consults with doctors who treat patients and perform surgeries at the hospital's eye clinic.

In the course of their investigations, researchers frequently discover something beyond expectation.

That's certainly the case for Smriti Agrawal, PhD, a former post-doctoral fellow in the HBI's multiple sclerosis research program. "I was 100 per cent sure I would be leading a lab at the University of Calgary or somewhere else," she admits. "Instead, I'm working with a major pharmaceutical company."

Agrawal is a member of the medical affairs team in the Department of Ophthalmology for Novartis Pharmaceuticals Canada. As a medical science liaison she serves as the scientific and research connection between the company and medical experts, traveling extensively to support doctors in Western Canada who treat patients and conduct clinical research related to diseases of the eye.

She advises clients about anti-VEGFs (vascular endothelial growth factor), a group of drugs that are effective in reducing blindness caused by macular degeneration. "Macular degeneration is most prevalent among older people, but also occurs in people in their thirties and forties who have diabetes or a blockage of the main retinal vein," Agrawal explains. "Anti-VEGFs reduce the excessive growth of blood vessels in the eye, helping to restore vision."

"Being immersed in research at the HBI has enabled me to grasp new knowledge quickly and stay current on scientific research and clinical trials that are relevant to my work."

And while the corporate environment may be a complete change from the research lab, Agrawal notes that her primary purpose is basically the same — educating and sharing knowledge with her medical and commercial colleagues at Novartis and the retina specialists whom she supports.

Pivotal to her success are the more than six years she spent at the HBI.

The collaborative environment at the institute honed her abilities to work with colleagues. As a research assistant professor, Agrawal developed and taught a new course for graduate students embodying teamwork in the process. Involving senior post-doctoral fellows as course instructors, she was able to encourage development of teaching skills in her fellow colleagues as well.

Agrawal also benefitted from career development activities including the HBI's Research, Education and Leadership in Neuroscience (REALISE) program that provides trainees and members with enhanced skill development and training opportunities. She credits the program with helping to expand her perspective as well as refining the necessary skills to be successful in her unexpected career path. As a testament to Agrawal's transition from education to business, she was invited back as a guest speaker to deliver a REALISE presentation 'From Academia to Industry,' sharing key learnings with HBI trainees based on her personal experiences.

Agrawal's current responsibilities include spearheading conversations among clinicians who are anti-VEGF researchers and ensuring they have access to the latest papers. If clinicians are interested in launching projects or being part of global trials, she becomes their champion. "I present their projects to our scientific affairs leadership team, advocate for them and recommend funding to keep their projects moving forward. The ultimate goal is always to add to the global scientific body of knowledge."

Her role, she says, relies heavily on the teaching and collaborative skills strengthened at the HBI. Agrawal recently received Novartis' Outstanding Collaborative Teamwork Award, recognizing her ability to work collaboratively and bring in information to ensure that her commercial team is aligned and knowledgeable. "You can never take the teacher out of someone," she says with a laugh. "This job is completely different from anything I've ever done, and the HBI was definitely a major factor in making it possible."

Building an institute-wide neurotechnologies platform

In a Q & A, Bruce Pike, PhD, shares insight into the strategy that will ensure the HBI continues to utilize state-of-the-art technology to advance discovery in brain and mental health.

Previously, Pike was the director of the McConnell Brain Imaging Centre at the Montreal Neurological Institute and a professor in the Departments of Neurology and Neurosurgery, Biomedical Engineering and Medical Physics at McGill University. He was recruited to the HBI and Department of Radiology at the Cumming School of Medicine as part of the Campus Alberta Innovates Program (CAIP), where he now holds the CAIP Chair in Healthy Brain Aging.

1) What is neurotechnology?

"Neurotechnology" is a relatively new term referring to any technology that enables researchers and physicians to understand how the brain works, to detect and monitor neurological and psychiatric diseases or to treat or repair the brain. Three broad classes of neurotechnologies are neuro-recording, neuro-stimulation, and neuro-informatics.

Neuro-recording techniques such as computerized tomography (CT) and magnetic resonance imaging (MRI) brain scans are used to observe and record the structure and function of the nervous system.

Neuro-stimulation involves the activation of part of the nervous system, by methods such as transcranial magnetic stimulation (TMS), transcranial direct current stimulation (TDCS), focused ultrasound, implantable devices and optogenetics (using light to control neurons that are genetically sensitized to light).

Making sense of the enormous amount of data we record, in addition to all of the behavioural and clinical information, is where neuro-informatics comes into play. Neuro-informatics includes cataloguing data, computational and processing tools, mathematical modelling and statistical analysis to facilitate greater understanding of the multi-level complexities of the brain.

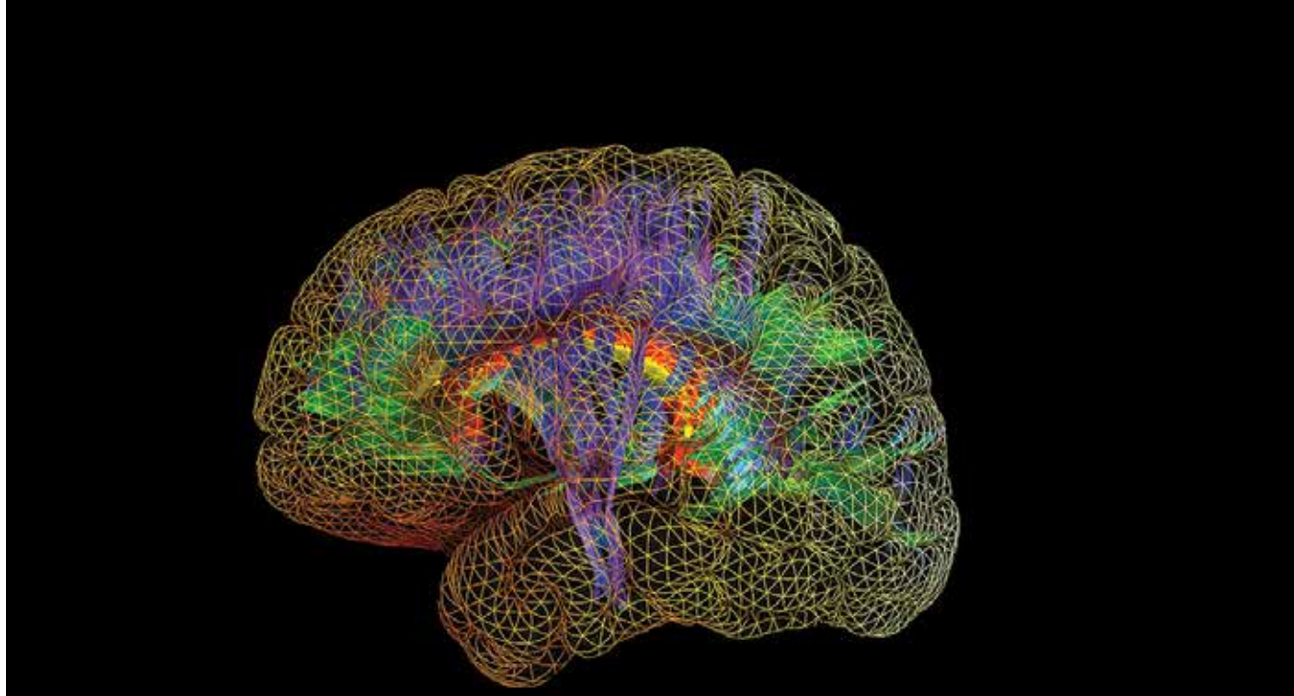
The HBI is developing three neuroscience technology platforms based on these classes to ensure our researchers have access to leading-edge infrastructure and technical expertise to support high-impact research.

2) How does neurotechology benefit brain and mental health research?

Advances in neuroscience have become inextricably linked with neurotechnologies.

For example, neuro-recording technologies provide researchers with unprecedented views of the awake, functioning brain and neuro-stimulation allows control of individual neurons to provide unique and detailed information on brain function.

Neurotechnologies have rapidly evolved in recent decades to revolutionize our understanding of the healthy human brain, how it develops and how it is affected by disease.



A mesh representation of the cortex of the brain, derived from a high-resolution MRI scan and software extraction package that performs a 3D mesh fit to the brain's surface. Photo credit: Bruce Pike, PhD, and Claude Lepage, PhD.

3) How does neurotechnology at the HBI benefit the community?

Fifty per cent of Canadian families are affected somehow by diseases or disorders of the brain. Neurotechnologies have transformed the diagnosis and treatment of neurological diseases in ways that were unimaginable in the past.

Much of what we can perform non-invasively today could only be achieved by opening the skull a few decades ago. Advances in neurotechnologies have dramatically accelerated drug discovery and the development of new treatment strategies that are saving the lives of millions of people and improving quality of life for millions more. For example, treatment of certain movement disorder patients using integrated brain imaging and stimulation technologies to target specific deep brain structures has already proven to be very effective.

4) What's one thing you think is going to change the face of brain and mental health research in the next 10 years?

Deep brain neurosurgery without breaking the surface of the skin is transformational.

I am particularly excited by the emerging brain imaging and stimulation techniques such as MRI-guided, high-intensity focused ultrasound (HIFU). This integrated technology makes it possible to precisely and selectively affect the tiniest and deepest portions of the brain in a non-invasive fashion. In addition to surgical applications, this has the potential to be a groundbreaking neuro-stimulation tool for highly personalized medical therapy as well as basic neuroscience research.

5) How is the HBI incorporating advances in neurotechnologies into its research programs?

The HBI is developing a strategy that includes a neurotechnology platform that will span the institute's entire research framework.

This institute-wide integration of neurotechnologies is one of the major forces that will continue to drive the HBI towards greater discovery in brain and mental health over the next decade. It will advance our ability to translate discoveries into innovative health care solutions, informing the development of strategies for detection, prevention and treatment of neurological diseases and disorders to ultimately improve brain and mental health in the community.

Our appreciation of Dr. Chen Fong's contributions to the HBI

By Samuel Weiss, PhD

It is fair to say that without the tireless contributions of Dr. Chen Fong, we would not have a Hotchkiss Brain Institute.

Beginning in the spring of 2003 — in close allegiance with Mr. Jack Davis, Dr. Grant Gall and Dr. Alastair Buchan — Dr. Fong was a founding father of the HBI. Not only was he instrumental in guiding and mentoring me, as the inaugural director, in developing a meaningful business plan for the HBI, Dr. Fong (then Head of the Department of Radiology) was able to help convince Harley Hotchkiss and the Hotchkiss family to invest their name and significant resources in the HBI. Beginning with our first anonymous donor who contributed $6 million that was matched, allowing us to launch four of our first five research programs, Dr. Fong has managed to bring many additional major donors and community members to see the virtues of supporting the HBI — with their financial support and personal time. As a result, we have developed an amazing family of community support that is second to none in the province of Alberta.

As if these contributions were not sufficient, Dr. Fong has personally contributed to the HBI's success in amazing ways. He has been a member of the HBI's Strategic Advisory Board (SAB) through the HBI's entire 10 years — for three years as head of the Department of Radiology and for the past seven years as SAB Chair. Although the HBI accepted the passing of the Chair torch to Mrs. Brenda Mackie this year, Dr. Fong continues to serve on the SAB (could not imagine it any other way!). Moreover, Dr. Fong created the Dr. T. Chen Fong Doctoral Scholarship in Neuroscience, which has funded dozens of remarkable neuroscience students over the past six years. His passion and commitment to innovation and excellence is thus impacting on students and faculty alike — as he gives so much of his time, wisdom and financial support to the HBI. Finally, in this regard, Dr. Fong was singularly a driving force in the recruitment of Drs. Bruce Pike and Ann Clarke — arguably one of the most significant and transformative joint recruitments to the University of Calgary in the past decade.

A personal editorial set of comments, if I may. Details notwithstanding, I consider it an honour and privilege to have been advised, mentored and supported by Dr. Fong for more than 11 years and counting. Few people I know combine wisdom, caring and humour in their generosity of time and spirit — as does my dear friend Dr. Fong. I consider myself fortunate to have met him and to have worked so closely with him over the years. Our institute, school, university, city, province and nation are made better by the selfless contributions of a small number of outstanding individuals. Dr. Fong is one of those — in fact, one of a kind!

Thanks, Chen — for all you have done and all you continue to do.

Stay Connected

Visit hbi.ucalgary.ca
Email hbi@ucalgary.ca
Find Hotchkiss Brain Institute on Facebook
Follow us @HotchkissBrain on Twitter
Phone 403.220.3558

Hotchkiss Brain Institute

Health Research and Innovation Centre, Room 1A10
Cumming School of Medicine, University of Calgary
3330 Hospital Drive NW
Calgary, AB T2N 4N1

Credits

Managing Editors: Kristy Cross, Julie Arnold, Janice Lee
Contributors: Alison Myers, Cathy Nickel
Photography: Bookstrucker Photography, James May Photographics
Design: Build Studio

HOTCHKISS BRAIN INSTITUTE
Improving brain and mental health in your community for 10 years

Improving brain and mental health in your community for 10 years.

hbi.ucalgary.ca