nova scotia health authority
Research Services

Research Focus

Not unlike the brain itself, the neuroscience research effort underway in Halifax, Nova Scotia is vast and complex. Clinicians, scientists, students and administrators affiliated with the Nova Scotia Health Authority (NSHA), Dalhousie University and the Brain Repair Centre (BRC) are conducting an array of studies addressing problems from the common—headaches, concussions, strokes, seizures, dementia—to the relatively rare: ALS, Huntington's disease, glioblastoma.

This research is essential. Disabling brain and nervous system disorders are on the rise, with profound impacts on the lives of individuals and families, the health care system and society as a whole. Researchers at NSHA are advancing our understanding of the nervous system in health and disease, while looking for practical solutions to challenges they see every day. This involves working with colleagues locally, nationally and internationally to develop and validate new strategies for diagnosing, treating, and preventing disease, as well as examining health care practices and systems and leading the way to transformational change.

Carefully Planned Surgery Provides Miracle Epilepsy Cure

Zack Logan first noticed strange rush-like feelings when he was a child. He didn't tell anyone, even though the feelings became more frequent and intense. It was only after he had a convulsive seizure, three years ago while working as a line cook at the Halifax Infirmary cafeteria, that Zack realized his earlier experiences had also been seizures.

"I was cracking an egg onto the grill and the next thing I remember, I was sitting in emergency in a wheelchair in my work clothes, with a badly burned forearm," recalls Zack, now 25. He's fortunate his co-worker, Rolanda Kane, noticed him leaning oddly over the grill. She ran to him, grabbed his arm off the grill and eased him to the floor before he fell face first.

Emergency physicians referred Zack to Dr. Mark Sadler, a neurologist who specializes in definitively diagnosing epilepsy by taking a careful history and examining the results of a variety of electro-

"Epilepsy was taking a toll and would have shortened my life," says Zack. "Now I feel great and was inspired by my experience to re-train for a new job."

physiology and imaging studies. These include MRI and EEG (electroencephalography) studies conducted over days or weeks in the Epilepsy Monitoring Unit (EMU). Dr. Sadler diagnosed Zack's epilepsy after just five days and located the source of the seizures in a small area of his right temporal lobe.

Former Halifax Infirmary line cook Zack Logan now works as a medical device re-processor at the hospital, sterilizing the very instruments Dr. David Clarke used to cure his epilepsy.

"Because the seizures were coming from a small area, I could have surgery to possibly cure my epilepsy," says Zack. "It was a scary prospect, but medications weren't controlling my seizures and Dr. Sadler made me feel confident, so I went ahead."

After thoroughly mapping Zack's brain to ensure surgery wouldn't disrupt vital functions, neurosurgeon Dr. David Clarke removed the area of misfiring neurons. Zack has been seizure free ever since. "Epilepsy was taking a toll and would have shortened my life," says Zack. "Now I feel great and was inspired by my experience to re-train for a new job."

neuroscience

Halifax First Seizure Clinic

Fast-Tracking to Treatment—and Research—After a First Seizure

Health care systems *can* be overhauled quickly and dramatically to provide more timely access to care. Internationally known epileptologist Dr. Bernd Pohlmann-Eden proved this when, within a year of launching the Halifax First Seizure Clinic in 2008, he and his small staff cut wait times for assessment after a first seizure from 6–8 months to 1–3 *weeks*.

"We re-organized everything so patients would be seen quickly after a first seizure," says Dr. Pohlmann-Eden, who runs the clinic with nurse practitioner Karen Legg. "This is critical, because risk of recurrence is highest in the first year after an initial seizure, which in turn puts people at risk of serious injury and affects their ability to drive and earn a living. And, research shows that early diagnosis and treatment positively impact the course of the disease."

The Halifax First Seizure Clinic is yielding another important result—data. "We're building a treasure trove of data," says Dr. Pohlmann-Eden. "We conduct a rigourous assessment including EEG and MRI scans, genetic testing, an in-depth history, psychiatric and cognitive screens and other tests that are giving us a detailed picture of the early course of epilepsy."

The data has also revealed strong connections between first seizure and anxiety, depression and marijuana use. "Many experts have thought that anxiety and depression in people with epilepsy are caused by the disorder and stigma surrounding it, but we believe these conditions arise before a first seizure because the neural network is already not functioning well," Dr. Pohlmann-Eden says. "The increased risk of seizure we found in people who smoke marijuana is difficult to disentangle, as they may be self-medicating for anxiety and depression, which we also consider risk factors for seizure."

Dr. Pohlmann-Eden's analysis is pointing the way to more accurate means of predicting response to treatment and risk of recurrence.

"Experts have long thought that congenital malformations of corticol development (MCD) found in MRI scans predict poor outcomes in epilepsy," he notes. "Our data show MCDs may have a good treatment response and favourable outcomes, at least in the early stages."

The data analysis has also found that people with pre-existing psychiatric conditions and asymmetrical amygdala (almond-shaped groups of neurons associated with fear responses and found in both halves of the brain) face a higher risk of seizure recurrence. "This kind of clinical and imaging information helps us make decisions about medication and whether we should send patients for EEG assessment to see if their epilepsy can be treated with surgery," Dr. Pohlmann-Eden says.

Dr. Pohlmann-Eden has literally put Nova Scotia on the world epilepsy research map, hosting an international epilepsy conference on the South Shore every second year that brings experts from around the world together to share information and brainstorm new approaches to epilepsy.

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Potential Help for Blinding Headaches

A rare condition known as Idiopathic Intracranial Hypertension (IIH) triggers terrible headaches and sometimes vision loss, as the pressure of the fluid that bathes the brain and spinal cord rises. Younger, overweight women of childbearing age are most often affected, but the causes of the condition are unknown. Neurologists Dr. Laine Green and Dr. Charles Maxner are working with neuroradiologist Dr. Jai Shankar and ophthalmologists Dr. Anu Mishra and Dr. Wesley Chan to see if blood vessels are involved. They've received funding from the Nova Scotia Health Authority Research Fund and Radiology Research Foundation to examine blood vessels in patients' brains using MRI. "If narrowing of the veins causes this disorder, perhaps we could stent them to release some of the pressure," says Dr. Green. "Or vasodilators might help. The first step is to learn how the veins are involved."

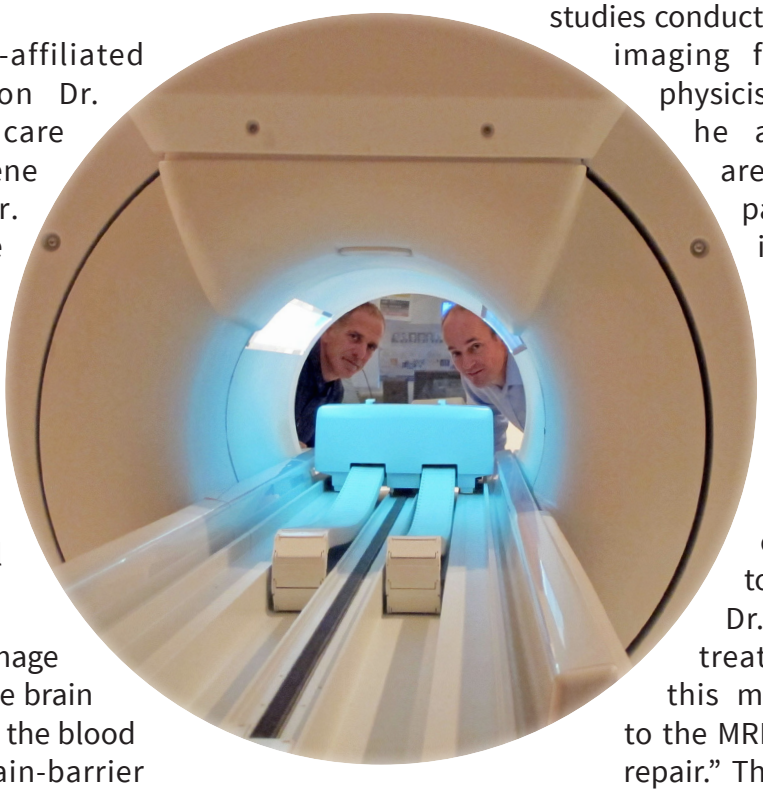
Special Thanks! to the departments of neurology & neurosurgery, medical device re-processing, the Brain Repair Centre & the BIOTIC facility

Preventing Epilepsy and Other Long-Term Effects After Brain Injuries

Traumatic brain injury will land a person in emergency in the short term—and may trigger serious long-term effects. These include an increased risk of developing epilepsy, as well as cognitive impairments, emotional problems and neurodegenerative diseases such as Parkinson's.

NSHA and Dalhousie-affiliated clinicians—neurosurgeon Dr. David Clarke, critical care specialist Dr. Rob Greene and radiologist Dr. Matthias Schmidt—are working with Dalhousie Medical School scientist Dr. Alon Friedman and BIOTIC (Biomedical Translational Imaging Centre) to develop new strategies for preventing these dismal consequences.

"The essential issue is damage to the blood vessels in the brain that allows substances in the blood to cross the blood-brain-barrier (BBB) and enter the nerve tissue, where it can cause a lot of problems as time goes on," Dr. Friedman says.



Dr. Alon Friedman and Dr. Chris Bowen look through the 3T MRI at the BIOTIC facility in Halifax.

"We want to know if we can actually prevent epilepsy and other problems by identifying and treating this microvascular damage soon after the initial injury."

Dr. Friedman has already found that a safe and proven blood-pressure medication can repair the BBB in studies conducted at BIOTIC's preclinical imaging facilities with medical physicist, Dr. Chris Bowen. Now, he and his collaborators are enrolling brain injury patients in a study to see if the same medication can repair microvascular damage in humans.

"We're using the 3T MRI in the BIOTIC facility at the Halifax Infirmary first to locate and characterize any damage to the blood-brain-barrier," Dr. Friedman says. "After treating the patients with this medication, we go back to the MRI to assess the degree of repair." The Canadian Institutes of Health Research (CIHR) awarded the researchers close to $1 million in 2016 for this new clinical study.

Neuroscience Alliance Breaks Down Barriers to Create Better Patient Care

Over the past several years, the divisions of neurosurgery, neurology and orthopedic surgery (spine program) have come together to develop a collaborative plan for providing seamless, integrated care to Atlantic Canadians with diseases and disorders of the nervous system. In partnership with the QEII Foundation, they created the *Neuroscience Alliance* and the *Brain. Spine. Spirit.* campaign. This has raised $2.5 million to create a new intermediate neurosurgical care space, a comprehensive spine program, and an expanded epilepsy monitoring unit, and to purchase a robotic surgical arm for ultimate precision in open-brain procedures. Enhanced clinical integration will pave the way to more collaborative research to further improve patient care and outcomes in the future. For more information, visit:
http://thechronicleherald.ca/qe2times/research-innovation/1371977-the-academic-neuroscience-program

Saving Lives and Preventing Disability in Stroke

Stroke patients across Nova Scotia are gaining access to transformational advances in post-stroke care, thanks to clinical trials and health-systems research at NSHA. More people are surviving, with less disability, than experts could have dreamed possible just a few years ago. "We're seeing the greatest advance since clot-busting thrombolysis came on the scene 20 years ago," says senior stroke neurologist Dr. Stephen Phillips.

This advance is a technique known as EVT—endovascular thrombectomy—in which an interventional radiologist threads a catheter into the patient's brain through an artery in the leg. The catheter is equipped with a wire stent that becomes enmeshed with the clot so that it can be extracted from the blood vessel.

"The results are astonishing," says Dr. Jai Shankar, the interventional neuroradiologist who performed the first EVT in Nova Scotia on Christmas Day, 2011. "People were wary because it was a so-called experimental technique at the time, but when they see my videos of speechless and immobilized people sitting up and talking, minutes after the procedure, they are convinced." Dr. Phillips and Dr. Shankar co-led NSHA's participation in the ESCAPE trial, a Canadian-led international study comparing EVT plus thrombolysis (standard care) to thrombolysis alone. The results were published in *The New England Journal of Medicine* in 2015 .

"Adding EVT to thrombolysis dramatically reduced disability and also cut the death rate by 50 per cent in the ESCAPE trial," says Dr. Shankar. "So now EVT is the new standard of care." The challenge is to make EVT accessible to all Nova Scotians, since the specialists and equipment required are located in Halifax and—given that two million brain cells die every minute after a brain-artery blockage—time is of the essence when it comes to stroke.

"We're seeing the greatest advance since clot-busting thrombolysis came on the scene 20 years ago."

"We're looking at practices and processes to determine how we can most efficiently identify eligible patients and get them to Halifax within five hours of symptom recognition," explains stroke neurologist Dr. Gord Gubitz.

Dr. Gubitz and Dr. Shankar are co-leading NSHA's involvement in a new Canadian Institutes of Health Research (CIHR)- funded clinical trial of a neuroprotective agent that could protect stroke patients' brains between the onset of symptoms and treatment in hospital. "Paramedics will administer the new drug on the way to hospital to help salvage the non-functioning parts of the brain before permanent damage occurs," says Dr. Phillips. "If the drug proves successful in this situation, we will have yet another tool for improving outcomes in the face of rising stroke rates."

Interventional neuroradiologist Dr. Jai Shankar uses sophisticated x-ray imaging techniques to guide a catheter from an artery in the leg to a blood clot in a stroke patient's brain, to extract the clot. In addition to his work improving stroke outcomes, and other research projects in such areas as intracranial aneurysms, vascular malformations, brain tumours and MS, Dr. Shankar is pioneering the use of CT perfusion scans to accurately confirm brain death. CIHR has awarded him close to $1 million to refine the protocol and develop guidelines to help clinicians across Canada make medically, ethically and legally sound recommendations for non-responsive patients.

Averting the Dangerous Consequences of Aneurysm

An aneurysm is a bulge in the wall of a blood vessel in the brain. As many as three people in a hundred have small aneurysms that may never act up. In less common cases, the rupture of a larger aneurysm can cause severe disability or even sudden death. "Aneurysms don't typically produce symptoms unless they rupture… they're most often discovered in brain scans for other issues, such as headaches or concussions," says cerebrovascular neurosurgeon Dr. Gwynedd Pickett. "The challenge is in deciding how to manage the risk, once we know someone has an aneurysm."

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As Dr. Pickett explains, risks of treatment may outweigh benefits. In these situations, it's better to monitor the aneurysm and intervene only if something changes. In other cases, clinicians must choose the safest and most effective method of preventing a rupture.

"The traditional method is to open the skull, find the affected blood vessel, and clip the neck of the bulge to prevent blood from flowing in and causing a rupture," says Dr. Pickett. "The newer method uses x-ray-guided catheters to access the blood vessel via an artery in the leg, and pack the bulge with platinum coils to prevent it from filling with blood."

Some aneurysms do not feature a defined "bulge" but, rather, the entire circumference of the blood vessel is distended. Dr. Jai Shankar is helping to pioneer the use of stents called flow diverters to prevent these risky and previously untreatable aneurysms from rupturing. He has brought specialists from across Canada together to learn the method and pool their data into a rich source of technical and clinical knowledge.

"We're evaluating the outcomes of each procedure over time, internationally," notes Dr. Pickett. "At the same time, we're evaluating the tools we use locally to guide our clinical decision-making, so we can adjust them if need be and share them with others with confidence."

Dr. Pickett and Dr. Shankar are also working with research coordinator Judith Jarrett, RN, on an NSHA-funded study to see if CT perfusion scans can help them better predict a dangerous consequence of aneurysm rupture known as vasospasm. This tightening of blood vessels in the brain limits oxygen and can trigger a stroke. "If we could predict who's at risk, we could intervene early to save lives and prevent disability," says Dr. Pickett.

Dr. Pickett holds a platinum coil (left) and clips (right) used in the treatment of aneurysms.

Alzheimer's Disease

Dr. Sultan Darvesh holds a spinal cord (left) and donated brain tissue (right).

Creating the World's First Definitive Diagnostic Test for Alzheimer's Disease

Halifax researchers are on the verge of launching the first-ever technology with the ability to definitively diagnose Alzheimer's disease in a living person's brain. "Until now, the only way to confirm this diagnosis was to have the brain examined by a neuropathologist after death," says Dr. Sultan Darvesh, the NSHA-Dalhousie neurologist who is the brains behind the breakthrough technology.

"We have access to a large network of collaborators and investors through Treventis," notes Dr. Darvesh. "After many years of laying the groundwork, we are really gaining traction now."

For more than 20 years, Dr. Darvesh has examined the donated brains of healthy people and those who have died with dementia, looking for clues to diagnosing and treating Alzheimer's disease. He established the Maritime Brain Tissue Bank in 1994 as a means of methodically storing and studying the brain tissues and health histories of their donors.

"We confirmed that an enzyme called butyrylcholinesterase, or BChE, accumulates in the plaques and tangles in Alzheimer brains," says Dr. Darvesh, named Dalhousie Medical Research Foundation-Irene MacDonald Sobey Chair in Curative Approaches to Alzheimer's disease in 2014. "When we found that it ignores similar plaques found in normal brains, we realized we had discovered a unique marker of Alzheimer's disease."

When Dr. Darvesh and his team found a compound that binds with BChE in the living brain and lights up in PET and SPECT scans to reveal the presence of

Alzheimer-specific plaques, they partnered with BIOTIC to test the potential diagnostic technology in pre-clinical models of Alzheimer's disease.

With the success of these Canadian Institutes of Health Research- and Brain Repair Centre-funded studies, Dr. Darvesh and BIOTIC moved on to planning MRI studies of people with Alzheimer's disease—the next all-important step on the way to commercializing the technology.

"The lack of a tool for diagnosing Alzheimer's disease in the living brain has led to the failure of all clinical trials for an anti-Alzheimer drug to date," says Dr. Darvesh. "With a diagnostic tool in hand, we will have the means to see which drugs are working to halt or reverse the disease. Then we will have the diagnostic and therapeutic power to prevent an epidemic."

As it happens, Dr. Darvesh has found that BChE plays an active role in the Alzheimer's disease process. He's working now with collaborators at Treventis Corporation to identify a compound that will block BChE and prevent Alzheimer from taking hold. Dr. Darvesh co-founded Treventis in 2010 as a vehicle for commercializing diagnostics and therapeutics for Alzheimer's disease and other forms of dementia and runs the diagnostic arm of the company out of Halifax. Its therapeutic arm is based in Toronto.

"We have access to a large network of collaborators and investors through Treventis," notes Dr. Darvesh. "After many years of laying the groundwork, we are really gaining traction now."

Maritime Brain Tissue Bank

One of only three well-established brain banks in Canada, the Maritime Brain Tissue Bank has received more than 1,000 brains, donated by people in the Maritimes affected by Alzheimer's disease, dementia, ALS, epilepsy, Parkinson's disease, multiple sclerosis, spinal cord injury, cerebral vascular disease, schizophrenia and other diseases of the brain and nervous system. It is an invaluable resource for the growing neuroscience research community in Halifax, as well as for researchers around the world, to probe the nature and causes of neurologic and psychiatric diseases.

A recent expansion of the brain bank, funded by Dalhousie Medical Research Foundation's 2014 Molly Appeal, enables researchers to investigate the brain at the molecular level, revealing a wealth of crucial information about disease processes and how these could be influenced to stop disease. This is particularly important in the Maritimes, where the aging population faces an ever-growing burden of brain and nervous system disease.

For more information about the Maritime Brain Tissue Bank, and how to plan to make a tissue donation, visit: **http://braintissuebank.dal.ca**

BIOTIC helps NSHA Researchers Pioneer New Neurotechnologies

The Biomedical Translational Imaging Centre (BIOTIC) is a crucial resource for neuroscience researchers in Halifax. Located in three facilities at the QEII Health Sciences Centre and IWK Health Centre, BIOTIC houses one of Canada's most extensive arrays of biomedical imaging equipment. Several of these technologies—such as high-powered MRI, EEG and MEG (magnetoencephalography), provide detailed functional and structural information about the brain that is essential for developing diagnostic tools and therapeutic strategies for brain diseases.

BIOTIC's team of scientists, engineers, technicians and project managers is working with several NSHA researchers on brain-related technologies. These include partnerships with major multinational corporations to develop new MRI and MEG applications for mapping the brain. "We're improving the accuracy of pre-surgical brain mapping, so surgeons can go in to remove a brain tumour, or the source of epileptic seizures, without fear of disrupting vital brain functions like the ability to speak, process language or control one's limbs," explains BIOTIC's scientific lead, Dr. Steven Beyea, a physicist in the Department of Diagnostic Radiology at Dalhousie and NSHA.

BIOTIC plays a crucial role in many other neuroscience projects, including Dr. Sultan Darvesh's push to develop a diagnostic test for Alzheimer's disease, Dr. Alon Friedman's work to diagnose and repair damage to the blood-brain-barrier, and Dr. Shaun Boe's efforts to create an EEG-based tool to help people restore motor abilities following a stroke. "While we work in many areas besides the brain, we have the particular expertise and equipment to make vital contributions in neuroscience," notes Dr. Beyea. "It's very satisfying to be involved in these projects."

MS & Huntington's Disease

The Face of MS in Nova Scotia

With access to the longest-running provincial MS database in Canada, NSHA-Dalhousie MS researchers can paint a clear picture of the evolution and impact of MS in Nova Scotia.

- More than 250 of every 100,000 Nova Scotians have MS .
- The ratio of women to men with MS has shifted from 2:1 to 3:1 today.
- MS is frequently accompanied by cognitive problems, fatigue, anxiety and depression.
- MS patients suffer disproportionately high rates of other health problems, including hypertension, hyperlipidemia, diabetes, heart disease, chronic lung disease, and epilepsy, demanding a comprehensive approach to managing the patient's overall health in partnership with primary care.

Hope for Huntington's Disease

As potential new treatments for Huntington's disease emerge, clinicians in NSHA's multidisciplinary clinic are preparing for clinical trials. "Huntington's is an inherited neurodegenerative disease that causes uncontrollable movements and cognitive and psychiatric problems," says neurologist Dr. Kerrie Schoffer. She and fellow neurologists, Dr. Heather Rigby and Dr. Roger McKelvey, neuropsychologist Dr. Shannon Johnson, nurse Donna Bouchard and Huntington's Society social worker Barb Horner help more than 100 Huntington's patients and their families cope with the disease. They're involved in Enroll-HD, a multinational study of Huntington's risk factors, early warning signs, natural history and treatment effects. Drs. Schoffer, Rigby and McKelvey have also worked with Dalhousie scientist Dr. Harold Robertson on studies aiming to identify early markers of Parkinson's disease—such as changes in the sense of smell—that could be used to diagnose the disease in earlier stages when treatments may have more effect.

Blazing Trails in Understanding and Treating MS

Multiple sclerosis patients across Nova Scotia have access to top-notch comprehensive care through the Dalhousie MS Research Unit, established in 1981 by former Dean of Medicine Dr. Jock Murray.

"We've been clinical research leaders in MS for so long, our patients benefit enormously from our depth of knowledge and experience," notes Dr. Virender Bhan, head of the Division of Neurology at NSHA and Dalhousie Medical School.

The MS clinic neurologists, nurses and nurse practitioner Trudy Campbell together follow 2,000 MS patients at any given time, overseeing their care, collecting comprehensive data about their overall health and progression of disease, and involving them in international clinical trials of groundbreaking new treatments.

"We've played an important research and advocacy role in the approval and introduction of new disease-modifying drugs, including the first oral medications for MS," says Dr. Bhan. "These are so much easier for patients to manage than the injectables. We've been able to prove their real-world effectiveness—not just in clinical trials but in outcomes studies showing meaningful improvements in patients' functional abilities and quality of life over time."

The researchers are in now the early stages of clinical trials of potentially revolutionary new drugs. "This new generation of medications has the potential to repair damaged myelin and promote the remyelination of the nerves," says Dr. Bhan. "This is truly a new frontier."

Dr. Bhan and Ms. Campbell work closely with NSHA-Dalhousie neuropsychologist Dr. John Fisk, who involves patients in imaging studies to learn how MS affects the structure and function of the brain. With funding from Dalhousie Medical Research Foundation, he's

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working with BIOTIC to find applications for new MRI sequences that can detect MS-related brain changes, including microscopic damage to the white matter. Functional MRI is allowing the researchers to determine how this damage effects patients' information-processing efficiency in complex cognitive tests.

"Not only will these new imaging technologies help us better diagnose and understand MS," says Dr. Fisk, "they will help us monitor disease progression and response to treatment."

Research coordinator Margo MacFarlane shows patient David Smith how to use a handheld spirometer, used in a study assessing respiratory function in people with ALS.

Meeting Day-to-Day Challenges of Life with ALS

The search is still on for a drug that stops the motor neuron and synapse-killing processes of ALS (amyotrophic lateral sclerosis). Only one drug so far has shown a disease-modifying effect, with modest impact on survival. Progress is being made, however, on medications to manage the effects of ALS.

"By managing key symptoms, such as difficulty swallowing and breathing, we can extend average life expectancy from three to four years..."

"We saw positive results in one recent international trial of a potential muscle-strengthening drug, which led us to embark on a second trial," says NSHA-Dalhousie neuromuscular neurologist Dr. Ian Grant. "It may strengthen the breathing muscles, which is crucial in ALS, where respiratory failure due to weakness in these muscles is the leading cause of death."

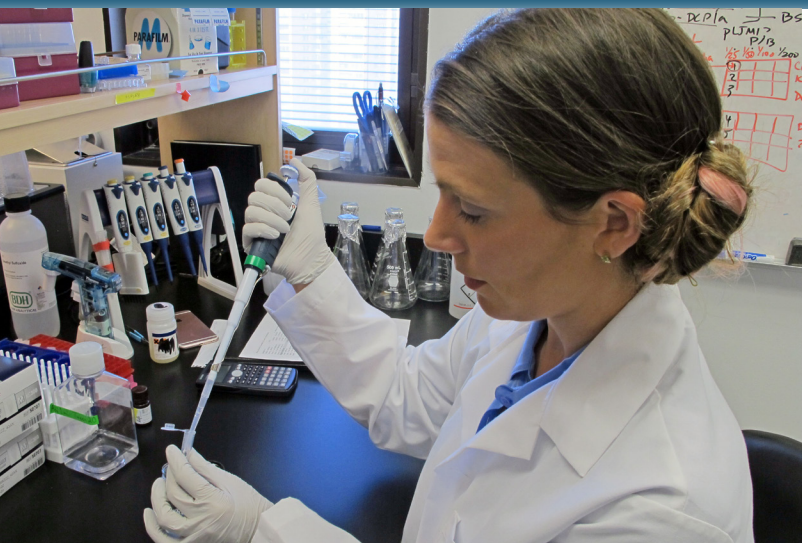
Dr. Grant and colleague Dr. Tim Benstead follow 30 to 40 patients at any given time in the ALS clinic at the Nova Scotia Rehabilitation Centre. They're building on a provincial ALS database begun in the 1970s. Working with research coordinator Margo MacFarlane, RN, they hope to involve patients in as many studies as possible.

"We're part of the Canadian Neuromuscular Diseases Network and the Canadian ALS Research Network," notes Dr. Grant. "By pooling our data and resources, we're able to bring more trials to Canada than we could working alone."

Dr. Benstead, meanwhile, is working with neurology resident, Dr. Caitlin Jackson-Tarlton, to study current and best practices in tube feeding in ALS. They will use this data to develop new clinical practice guidelines for use across Canada. BiPAP, or bilevel positive airway pressure, is another important supportive care measure for people with ALS.

"By managing key symptoms, such as difficulty swallowing and breathing, we can extend average life expectancy from three to four years, while improving quality of life for people with ALS," Dr. Benstead says. "There is still a long way to go, but at least we can help our patients live better day to day."

Glioblastoma



Dr. Adrienne Weeks holds some of the tools she uses while doing research in Halifax.

Stemming the Deadly Infiltration of Glioblastoma

Every week, neurosurgeon Dr. Adrienne Weeks delivers the devastating news to someone that they have brain cancer. Many have glioblastoma, the most common malignant primary tumour.

"Tragically, glioblastoma is typically fatal in two to five years," says Dr. Weeks. "It's horrible when you have to tell people they're going to die. That's why I go to the lab."

Dr. Weeks began exploring the mechanisms of glioblastoma invasion while doing a PhD in neuro-oncology at the University of Toronto, in conjunction with her neurosurgery residency. Now, as a QEII staff surgeon and assistant professor in Dalhousie's Division of Neurosurgery and Department of Medical Neuroscience, she continues that work in Halifax.

"Glioblastoma is a particularly difficult cancer to treat because it's not confined to a single area in the brain," she says. "It arises from astrocytes, fibrous star-shaped cells that form the supportive matrix of the brain. Once cancerous, these cells send spider-web-like strands throughout the brain. You can't cure these tumours with a scalpel… you can take out the core, but you can't get the tentacles."

Dr. Weeks does surgically remove glioblastomas, when the core is in an operable location: "We don't want to blind or paralyze people but, when we can, we remove as much of the tumour as possible, to take pressure off the brain, possibly prolong life, and improve quality of life."

Thanks to Maritimers' willingness to participate in research at NSHA, Dr. Weeks is able to take cancerous cells from patients and culture them into models of glioblastoma in her lab. She and her team are closely examining the role of RNA stress granules. These are tiny particles of RNA and proteins that form when the brain is under stress, creating a protective barrier around healthy and cancerous cells alike.

"We've found that RNA stress granules protect the cancer cells from radiation and chemotherapy," explains Dr. Weeks. "So, we're testing ways of weakening this shield to make the cancer cells more susceptible to treatments, without affecting healthy brain cells."

Dr. Weeks and masters student Dr. Aaron Robichaud (who is also a neurosurgery resident) have devised a strategy of infecting glioblastoma cells with a virus to knock down the gene that makes RNA stress granules. They believe this will strip the cancerous cells of their protection. To test this strategy in a living system,

"It's horrible when you have to tell people they're going to die. That's why I go to the lab."

Dr. Weeks is collaborating with Dr. Jason Berman, a pediatric hematologist-oncologist and leading zebrafish researcher, to create zebrafish models of glioblastoma. These models will open doors to new avenues of glioblastoma research in Halifax.

"Ultimately, my goal is to have something more to offer to patients," says Dr. Weeks. "If we can make the tumours more susceptible to treatment, target drugs more precisely to cancer cells, or personalize treatments to a person's specific form of the disease, we will have come a long way."

Setting a New National Standard for Pituitary Tumour Care

NSHA is home to the first team in Canada to take a multidisciplinary approach to pituitary tumours.

"Our model of care has become the envy of the country," says Dr. David Clarke, who heads the Division of Neurosurgery at NSHA and Dalhousie Medical School. "For the past two years, we've been giving workshops to colleagues across Canada who want to emulate the Halifax Neuropituitary Program's model of care."

While most pituitary tumours are not malignant, they pose complex challenges requiring input from a wide range of professionals. As co-directors of the Halifax Neuropituitary Program, Dr. Clarke and endocrinologist Dr. Ali Imran assembled a team that includes otolaryngologist Dr. Emad Massoud, ophthalmologist Dr. Aditya Mishra and neuroradiologists and radiation oncologists Dr. Liam Mulroy and Dr. Dorianne Rheaume. The Halifax Neuropituitary Program provides coordinated multidisciplinary care to approximately 1,800 patients from across Atlantic Canada in one central location.

"Our model of care has become the envy of the country"

Not only does the bean-sized pituitary gland control all other hormones in the body, it is located near the base of the brain between two carotid arteries and adjacent to the optic nerves. It's a delicate matter to remove the tumours but leaving them in place can have terrible consequences. Dr. Clarke and Dr. Massoud conduct the procedure using scopes and instruments threaded into the base of the brain through the nose. In most cases, the surgery leaves no incision and the patient's hospital stay is one to three days.

"In some people, the tumour prompts the pituitary to overproduce growth hormone," notes Dr. Clarke. "As a result, excess tissue accumulates over time, enlarging and coarsening their facial features and making their hands and feet bigger. We have shown that this can also have profound psychological effects."

Dr. David Clarke and Dr. Emad Massoud

Their proximity to the optic nerves means pituitary tumours can cause vision loss—usually gradual, but sometimes sudden. They can also trigger weight loss or gain, menstrual changes, sexual dysfunction and a host of other problems.

"Because we've consolidated so many diverse areas of expertise into one program, we can study the wide-ranging effects of these tumours over time," says Dr. Clarke. "We are following our patients in a rigourous way, recording all findings in a detailed database. This helps us to provide the best care whether this involves surgery, hormone replacement therapy, psychological support or watchful waiting. It also helps us to publish our findings so that others can learn from our experience."

The Halifax Neuropituitary Program is expanding its research efforts and aims to add a PhD-trained basic scientist to the program.

"Shedding light on the molecular mechanisms of pituitary tumours is the only way to discover potential targets for therapies that could prevent or at least mitigate their long-term effects," says Dr. Clarke. "We see basic science research as a natural extension of our comprehensive approach."

Charting a Rapid Pathway to the Right Care for Spine Problems

NSHA spinal neurosurgeons have joined forces with spine surgeons in orthopedics and colleagues in rehabilitation and chronic pain to create a comprehensive spine program. One of their primary goals is to develop pathways to care that will put people with spinal problems in front of the clinician who can help them most, quickly.

"As many as 90 per cent of people referred to a spine surgeon for elective surgery do not ultimately need the surgery," says Randi Monroe, director of Neurosciences Services for central zone in NSHA. "We're planning to revamp the system so that people's spines will be thoroughly assessed by professionals other than surgeons far earlier in the care pathway, so those who need surgery will see the surgeon much sooner, and those who do not will receive appropriate non-surgical care—such as physiotherapy—also much sooner."

Monroe and spinal neurosurgeon Dr. Sean Christie are co-leads on a Translating Research into Care (TRIC) grant they received from the QEII Foundation to lay the groundwork for this new system of care. "We're engaging providers and patients to examine the current system and see what steps we can take to improve our processes and outcomes," notes Dr. Christie, associate professor and director of research in the Division of Neurosurgery. "For example, we're looking at such strategies as education and screening tools to help family doctors and nurse practitioners evaluate patients more thoroughly in primary care, before referring to the spine program."

Patient education is another gap that needs to be filled, according to Monroe. "People need to be more prepared going into surgery, through specific lifestyle changes, having equipment in place, and customized exercises that will help them optimize their results,"

"We're engaging providers and patients to examine the current system and see what steps we can take to improve our processes and outcomes"

she says. "Those receiving non-surgical care also require information and tools to help them receive the full benefit of their treatments."

Nurse practitioner Angela Meagher (right) demonstrates assessment techniques on occupational therapist Amira Tawasky. Patient's spines are assessed to help determine the appropriate care path—to non-surgical treatment or a surgeon.

Navigating the Murky Waters of Physician-Assisted Death

With new federal legislation in place making it legal for physicians to actively help suffering patients end their lives, many are struggling to reconcile the new legal framework with their own personal and professional convictions. To better understand how neurosurgeons feel about the new legislation, the Canadian Neurosurgical Society (CNSS) asked NSHA-Dalhousie spinal neurosurgeon Dr. Sean Barry to lead an investigation.

"Because of the conditions we treat, neurosurgeons often care for patients who express a strong desire to die," says Dr. Barry, an assistant professor in the Division of Neurosurgery with a master's degree in ethics. "These could be people with terminal brain tumours, paralysis or neurodegenerative disease. We've been doing everything we can to help them, for years, but never before have we been in a position to actively assist them in dying."

"Overall, [survey participants] feel that making the practice legally acceptable does not necessarily make it morally or ethically acceptable."

To find out what neurosurgeons think of the new legislation and how it will impact their practice, Dr. Barry designed a survey and sent it to more than 200 neurosurgeons across Canada. More than 40 per cent responded.

"The vast majority of respondents accept the new legislation as inevitable, although 10 per cent strongly oppose it and only 20 per cent said they would be willing to be actively involved," reports Dr. Barry. "Overall, they feel that making the practice legally acceptable does not necessarily make it morally or ethically acceptable."

According to Dr. Barry, who wrote and presented a position paper based on his findings at the CNSS 2016 annual meeting, respondents expressed grave concerns. "They are troubled by the lack of clarity for defining when a physician-assisted death is allowable," he explains. "They feel every effort must first be made to ensure patients understand all treatment and palliative care options, and every institution must have strong measures in place to ensure every instance of physician-assisted death meets clearly defined conditions."

The CNSS supports members' right to abstain from active involvement in a patient's death. "We are not professionally obligated to participate and can take the position of conscientious objector," Dr. Barry says. "At the same time, every surgeon has the right to help a patient end their suffering if they feel it is truly in the person's best interest."

Dr. Barry is now investigating patients' attitudes. "As a spinal neurosurgeon, I've worked with many people who've wanted to die in the aftermath of a spinal cord injury," he says. "Several years later, however, they're happy to be alive and I'm so glad I was never called upon to help them end their life. It's an incredibly complex issue that needs to be thoroughly examined."

The Science of Spinal Cord Injury

Dr. Sean Christie and Dr. Saranyan Pillai are unravelling the chain of molecular events that follow traumatic spinal cord injury. "The initial injury unleashes a series of secondary events, such as inflammation and vascular changes, which in turn contribute to the loss of movement and such functions as bowel and bladder control," Dr. Christie explains. "If we could interrupt this process we could reduce the impact of the injury on people's lives." He and Dr. Pillai are analyzing spinal fluids obtained with consent from patients at different time points following a spinal cord injury, with help from research coordinator Lisa Julien.

Neurobiology of Vision Loss and Aging

Monitoring Cell Death in Glaucoma

A Canadian leader in glaucoma research, Dr. Balwantray Chauhan recently received a $670,000 project grant from the Canadian Institutes of Health Research (CIHR) to learn how retinal ganglion cells change and die in glaucoma, an increasingly common disease that gradually diminishes the peripheral vision and eventually leads to blindness.

"Retinal ganglion cells are specialized neurons that carry visual messages from the eye to the brain," explains Dr. Chauhan, professor and research director in the Department of Ophthalmology & Visual Sciences and an affiliated scientist at the QEII Health Sciences Centre. "As they die, the brain has an increasingly difficult time interpreting input through the eyes."

"As [the retinal ganglion cells] die, the brain has an increasingly difficult time interpreting input through the eyes."

Using novel imaging techniques and experimental models of glaucoma, Dr. Chauhan and his team will trace the progressive death of retinal ganglion cells and the resulting changes not only in visual function but in the shape and function of individual cells. This research will shed light on the mechanisms of glaucoma, while guiding clinicians in how to monitor glaucoma in their patients.

Using the Eye as a Window to the Central Nervous System

The eye may be the window to the soul, metaphorically, but it is also literally the window to the brain.

"We can see the retinal ganglion cells, which are part of the central nervous system, using imaging techniques that let us monitor changes in living eyes over time," says Dr. David Clarke, who heads the Division of Neurosurgery. "This makes the eye a fantastic model for studying the central nervous system as a whole."

In his lab at the Brain Repair Centre, Dr. Clarke and Dalhousie graduate students study the mechanisms of neuron survival and response to injury, using pre-clinical models of the visual system. Among many findings, they've discovered that a molecule known as NCAM (neural cell adhesion molecule) plays a vital role in preserving eyesight with age.

"Margaret Luke, a PhD student in the labratory, has found that a lack of NCAM is associated with vision loss in aging" Dr. Clarke says. "This makes it a therapeutic target worth exploring, since age-related vision loss is a huge and growing problem in our society."

Dr. Clarke and his team have published findings about NCAM and various other molecules related to their ability to enhance neuron survival and regeneration in response to injury and degenerative disease.

"This kind of basic science inquiry is essential to our long-term prospects of solving one of the greatest challenges of neuroscience—how to maintain the function of neurons following injury and during aging," says Dr. Clarke. "It will take ongoing commitment from governments, universities, health care institutions and scientists to find and develop the effective strategies we need."

Creating High-Tech Training Tools for Optimum Neuro-Surgical Proficiency

There are thousands of surgical instruments and any given neurosurgical procedure could require hundreds of them. It's essential that OR staff—nurses, surgeons and students—know exactly which instruments are to be used, in what sequence, in every procedure. It's a tall order and one that Dr. David Clarke, head of the Division of Neurosurgery, is tackling with new high-tech training tools.

"We are developing an iPad-based technology to train neurosurgery residents and nurses in the instruments and procedures they will encounter in the OR," says Dr. Clarke. "Eventually, we will develop a more immersive simulated operating-suite environment, but this is the first step."

The Brain Repair Centre has awarded Dr. Clarke and his team a $30,000 Knowledge Translation Grant to field test the new training app, which will be commercialized in partnership with Conquer Mobile. BIOTIC's director of business development, Denise Lalanne, is facilitating the partnership with this B.C.-based firm, which is planning to set up a satellite office in Halifax from which to build this new business.

"We see the opportunity to become national and international leaders in developing and evaluating this kind of training technology," Dr. Clarke says. "The American Organization of Registered Nurses has already adopted a training module developed here. The expansion potential is huge."

Nurses and residents who've used the app say it helps them refresh their memory immediately prior to a procedure, helping every step run like clockwork once they're underway. "Superior efficiency in the OR saves time and reduces risk of error, which improves patient safety," says Dr. Clarke. "We are in an excellent position at the QEII to develop, implement and evaluate these technologies."

Translating the NeuroTouch Concept to Spinal Surgery

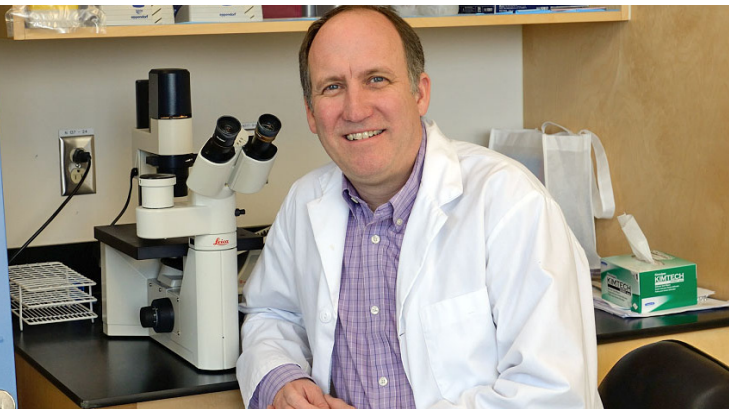
The world's first virtual reality brain surgery was performed by Dr. Clarke and his team at the QEII Health Sciences Centre in 2011 using the NeuroTouch brain surgery simulator. Since the recent commercialization of the NeuroTouch by CAE Inc, under the brand name Neuro VR, NSHA-Dalhousie neurosurgeons are turning their attention to spine surgery. Spinal neurosurgeon Dr. Jacob Alant and a team of computer science students are using gaming technologies to build 3-D simulation models of the spinal column and cord.

"Right now we're developing generic models that can be used to introduce neurosurgery residents to the spine," says Dr. Alant. "Eventually we aim to incorporate patient MRI and CT scans into the models, so they can be used to plan surgeries in advance and to navigate the spinal structures more safely and precisely during procedures."

With a track record of successful development of simulation-based educational initiatives, the Division of Neurosurgery is well-positioned to lead initiatives that use technology effectively to enhance the skills of the neurosurgery team so that it provide the best care to patients.

Health professionals use the iPad app to learn about instruments and procedures they will encounter in the OR

Brain Repair Centre Fosters Collaborative Action



Dr. Victor Rafuse is the director of the Brain Repair Centre. His own work focuses on how embryonic stem cells develop into functioning motor neurons, and how stem cells can be engineered into restorative therapies for people with central and peripheral nerve injuries, as well as neurodegenerative diseases such as ALS.

Halifax's dynamic neuroscience research community involves hundreds of individuals and dozens of teams, located in many different buildings and affiliated with several distinct institutions, including Nova Scotia Health Authority, the IWK Health Centre and Dalhousie University. The Brain Repair Centre (BRC) provides a unifying force that ties these diverse elements together to create a common vision.

"At the Brain Repair Centre, we are focused not only on connecting researchers with each other, but on connecting our researchers with the broader communities we seek to serve," says BRC director Dr. Victor Rafuse, a leading ALS researcher and professor in Dalhousie's Department of Medical Neuroscience. "We liaise extensively with patient advocacy groups and government agencies to ensure our research priorities align with the real needs of people in the community."

As one prime example, the BRC is working with the Government of Nova Scotia and the Brain Injury Association of Nova Scotia to develop a comprehensive strategy for addressing the complex needs of people recovering from traumatic brain injury. BRC leaders are also involved in shaping a provincial dementia strategy.

Over the past year, the BRC has established four research clusters—in the areas of traumatic brain injury, mobility disorders (the Atlantic Mobility Action Project), neurodegeneration, and neurodevelopment. "The clusters bring together researchers and clinicians with strong interests in these key areas, to map a strategy for growing stronger collaborative research efforts," notes Dr. Rafuse. "This is already helping us succeed in securing grants, recruiting top researchers, and connecting scientists to clinicians."

"At the Brain Repair Centre, we are focused not only on connecting researchers with each other, but on connecting our researchers with the broader communities we seek to serve"

Among its many programs, the BRC supports journal clubs, offers learning and networking sessions for members, hosts events that bring researchers together with the public and patient advocacy groups, and provides grants for discovery research, knowledge translation projects and scientific conferences. NSHA researchers who have received BRC grants include Dr. Gail Eskes, Dr. David Clarke, Dr. Sultan Darvesh, Dr. Shaun Boe, and Dr. Michael Schmidt. For more information, visit :

http://www.brainrepair.ca

nova scotia health authority Research Services

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