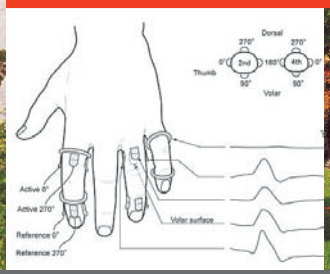
McGill Centre for Research on PAIN

Centre for Research on Pain

Newsletter



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BUILDING FOR THE **FUTURE**

McGill first became famous for its pain research when Ron Melzack and Pat Wall published their seminal Gate Control Theory in 1965. Since that time, McGill has continued to be a leader in pain research, but its impact on the world stage has increased dramatically in the last decade, as some of the top researchers from around the world have joined McGill. The McGill Centre for Research on Pain (MCRP) was founded in 2003 with the mission to create synergies amongst those working in the field at McGill and to support their research efforts in a number of practical ways.

In pursuit of this mission, the MCRP actively supports young researchers entering the field of pain research at McGill. Three new faculty recruits, Céline Gélinas, Laura Stone, and Michael (Mick) Sullivan, joined the MCRP in the past year and are profiled in the current newsletter. In addition to new faculty, the first five Post-Doctoral Fellows funded by a joint MCRP-AstraZeneca Canada program have been recruited from around the world to work on pain projects at McGill. These young scientists include Michael LaCroix-Fralish (Mogil Lab, genetics), Magali Millecamps (Coderre Lab, CRPS-1 models) Harunor Rashid, (Cervero Lab, central sensitization in models of chronic pain), Petra Schweinhardt, (Bushnell Lab, dopamine and the placebo effect), and Dave Seminowicz, (Bushnell Lab, changes to brain structure in chronic pain states).

Physically, the MCRP also continues to expand its size on campus. New labs for recent recruits have been established in the Genome Building thanks to the support of the Louise Edwards Foundation and to the partnership with AstraZeneca Canada. Added to the animal and human testing facilities reported on previously, this year will see the launch of a new small animal imaging facility, new microscopy facilities, an animal procedural bay, and wet labs for two faculty members. The Centre was also fortunate to secure the support of the Quebec Pain Research Network (www.qprn.ca) in establishing the animal behavioural testing facility and the small animal imaging facility as research platforms in this Network, augmenting the resources which these facilities will be able to draw upon, and securing their recognition as sources of technical expertise for pain researchers throughout the province.

The Centre expects that 2007 will see a continuance of the growth it has enjoyed over the last few years. To keep up to date with the most recent developments, stop by our website (www.painresearch.mcgill.ca) and see what is happening!

IN MEMORIAM

It is with great regret and sadness that the McGill Centre for Research on Pain announces the passing of Mr. Alan Edwards on Sunday March 11, 2007. As Director of the Louise Edwards Foundation, Board Member of the MCRP, and Director of Development for the MUHC Pain Treatment Centre, Mr. Edwards was a friend, colleague, and tireless supporter of pain research and treatment at McGill. He will be deeply missed by all.

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CÉLINE GÉLINAS:
HELPING THOSE WHO CANNOT SPEAK FOR THEMSELVES

Dr. Céline Gélinas thinks that just because an intensive care patient is unconscious does not mean that their body does not feel pain.

Dr. Gélinas, a member of the McGill Centre for Research on Pain, is leader of a research team on the evaluation of nursing interventions at the Groupe de recherche interuniversitaire en sciences infirmières de Montréal (GRISIM) and an assistant professor at the School of Nursing. She is also developing a way of evaluating pain in critically ill patients who are unable to communicate.

The world-famous McGill Pain Questionnaire assesses a patient's pain depending on their answers to questions, "but what happens when a patient cannot express themselves verbally?" Gélinas asked.

Dr. Céline GÉLINAS

"They're people and they deserve pain relief like everybody else."

"Until now, little research has been done on pain in unconscious patients. They can't answer questions verbally. And in that case, there is no other way of detecting the presence of pain except by looking for non-verbal clues, behaviour patterns and vital signs."

For the next four years, Gélinas will be fine-tuning the Critical-Care Pain Observation Tool (CPOT) which she developed. In addition, she will be working on pain management in critically ill adults.

She is a nurse with several years experience in Intensive Care Units in hospitals in Trois-Rivières and Quebec City and has worked with different categories of patients. She has also taught and done research at Laval University where she first developed the tool.

"In an Intensive Care Unit, patients may be unconscious because of drug therapy, illness or trauma," she said. "But many procedures can be painful. They tend to be intubated. They are attached to a breathing apparatus. Nurses have to turn them every two or three hours."

Research has shown that the most painful procedures that a patient can experience in an ICU occur when they are being turned or when they are suctioned to help them breathe.

"You often get visual clues from the patients," she said. "Facial expressions change. When they are being turned in bed, their body may become rigid. They may try to cover a painful place in their body with protective gestures. There may be problems with the way they respond to the ventilator, coughing and activating the alarms of the machine.

"Some of these clues could be related to other problems such as anxiety, delirium or worsening general health conditions," she said. "Physiological signs reflect stress and stress can be related to many different factors. Sometimes agitation is related to head trauma. Sometimes the tube and machine alarms are triggered by secretions.

"But the two most important non-verbal indicators of pain appear to be facial expressions and muscle tension."

And so far there has been no systematic way of assessing this pain.

Until now, nurses have been doing the best they can with clinical judgements and observations. Gélinas and her team are developing a systematic way of assessing the pain of patients in hospital ICU's and documenting their response to procedures. With the Critical-Care Observation Tool, nurses and other care-givers could look at the patient's body language and answer questions based on their own observations of a patient's pain.

"I also examined the way different nurses assessed the same patient at the same time, to discover if they saw the same things," she said. "Results are very positive. Nurses use the CPOT in very similar ways so the results are similar."

She wanted to see if there were observable differences when a patient was at rest and when they were exposed to a painful procedure like turning and discovered that during turning, patients responded with frowning, grimacing, coughing, tensing up or moving their hands towards the site of the pain. On a scale of zero to 10, patients experiencing more pain showed more reactions.

So far, she has tested the CPOT with two different groups – 105 patients recovering from cardiac surgery and 116 Intensive Care Unit patients recovering from a wide range of surgeries, trauma or medical conditions in several different sites. The tool was to assess both unconscious patients and others who were unable to speak but could express themselves with gestures.

She has made some interesting observations. Sometimes the amount of sedation affects the difference in pain expressed non-verbally. The higher the dose, the lower the reaction.

“And sometimes patients with head trauma react less intensively,” she said. “Brain injury may be a factor in the way people experience pain. That may be another promising line of research.”

Dr. Gélinas said that her priority is to support nurses with pain assessment in patients unable to communicate and encourage the wider use of the Critical-Care Pain Observation Tool in ICUs to help improve treatment in clinical practice.

She also wants to develop nursing interventions and measure their observable impact on the pain of ICU patients so that they that can be integrated in a pain management plan.

McGill, she said, is a place for her to grow.

“There’s great dynamism here,” she said. “The doors are open. You just have to come in and there are opportunities to work with great people.”

LAURA STONE:
BACK PAIN: DECIPHERING THE BIOLOGICAL PUZZLE

Back pain, migraine and arthritis or rheumatism are the most common forms of chronic illness among Canadians aged 60 and under and seriously limit the way that many people can live productively. The Canadian Pain Society estimates that chronic pain costs our economy $12.5 billion a year which is more than cancer, heart disease and HIV combined.

Dr. Laura S. Stone, a new, tenure-track assistant professor at the Faculty of Dentistry and a faculty member at the McGill Centre for Research on Pain, said that about 15 per cent of the population suffers from chronic lower back pain.

She thinks that if we can understand how the body changes when it experiences back pain, we can develop better ways of treating it.

“It can be thought of as a degenerative disease similar to arthritis and often involving muscle strain and the progressive breakdown of the discs between the vertebrae,” she said in a recent interview. “But mostly, it’s not clear what causes chronic back pain.”

“The broad, long-term goal is to better understand the biological details and use the information we discover to come up with better ways of dealing with it.”

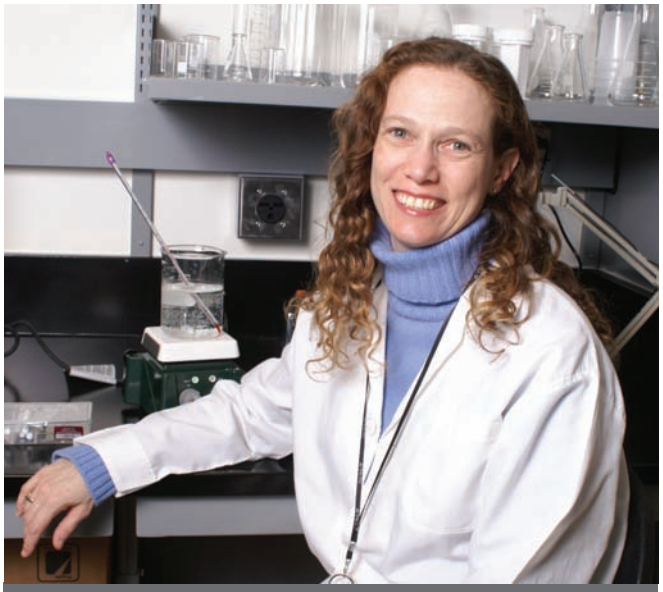
McGill, she said, is an ideal place to undertake such work.

A key factor in Dr. Stone’s decision to move here from the University of Minnesota was the Montreal Proteomics Network with its application of mass spectrometry technology including FTICR mass spectrometry to the characterization of proteins in a cell biological context.

She plans to combine traditional biochemical and anatomical research methods with analysis using some of the latest technology available in the world to identify changes – particularly to the proteins -- in the spinal fluid and discs of people suffering from chronic lower back pain.

Stone said 30 to 50 per cent of those suffering degenerative disc disease have no lower back pain “while a sub-set has severe pain.”

“I want to find out what makes them different.”



Dr. Laura STONE

The new technology may be significant. Conventional MRI imaging can diagnose degenerative disc disease by analysing factors like disc height. But it does not show any real relationship between the physical condition and pain or the lack of it.

“This may be because neuro-chemical or neuro-anatomical factors such as proteins, which are undetectable by imaging, contribute to the state of chronic pain,” she said.

“So proteomics is the really exciting part.”

“Traditionally we studied one aspect of proteins at a time. With proteomics, we can examine all of the aspects of all of the proteins together.”

Dr. Stone, who was born in Toronto, has a Ph.D. in neuroscience with a supporting program in pharmacology from the University of Minnesota-Twin Cities and a B.Sc. in chemistry and biochemistry from the University of California in San Diego.

She works with an orthopaedic surgeon who feels that spinal surgery is a serious intervention of last resort. The people she will study are among his patients.

Before and after treatment, a physiotherapist will examine the subjects, quantify the pain they experience and measure the extent of their functional impairment. And an anaesthesiologist will collect their spinal fluid.

"This could be important," she said. "Can a proteomic analysis of the fluid show why some people feel pain and others do not?"

Other members of the team will examine the material removed by surgery for physical abnormalities. "We know that pain-sensing nerve fibres grow and expand inside some discs," she said. "In some cases, the degenerating tissue sends out signals that it needs repairs and pain-sensing nerve fibres just seem to come in with the blood vessels and take over. We don't know why."

Other researchers on the team will examine similarities in disc degeneration between humans and rats. It is hoped that the information obtained will lead to new therapies – including new drugs – for these and many other chronic pain conditions and a better understanding of how existing therapies work.

Much of the research is based on very recent discoveries. The first reports on nerves in discs were published 10 years ago. Some of the technology she plans to use was developed only five years ago. She expects it will take two years to obtain 60 human subjects for study – 20 with chronic lower back pain, 20 with some degenerative tissue damage but no pain and 20 with no damage or pain – and obtain samples and another year to do the analysis.

"There are so many different questions that the answers could lead us in many directions," Dr. Stone said. "This is all completely unexplored."

But McGill is a place of "unparalleled opportunities" for the study of pain, she added.

"There is a critical mass of people here with a breadth of experience from a variety of backgrounds actively engaged in the subject, including experts in pain and in bone. There is moral support from the senior members of the Centre. There is a great collective energy in applied clinical research. And there are wonderful facilities."

MICK SULLIVAN
UNDERSTANDING HOW PAIN AFFECTS WHAT WE DO

Dr. Mick SULLIVAN

Mick Sullivan thinks that sometimes asking too many questions about a person's pain can make it worse.

That's Michael John L. Sullivan, Ph. D (Concordia), the professor of psychology and medicine at McGill University, holder of a Canada Research Chair in Behavioural Health, member of the McGill Centre for Research on Pain, and clinical psychologist with the University Centre for Research on Pain and Disability, who was nominated best Country artist for the East-Coast Music awards in 1999 while he was teaching and doing research at Dalhousie University in Halifax.

"There's a difference between feeling pain and expressing it," Dr. Sullivan said. "It's multi-dimensional and very complicated. I'm really interested in pain as it is reflected in behaviour, in how pain affects what people do."

In one experiment, he asked people suffering from lower back pain to participate in a performance-assessment test, lifting buckets filled with material of different weights lined up before them in rows on a table. Later he asked them to undertake the same tasks after asking them about their pain and how much it hurt. For many participants, the amount they were able to lift declined dramatically.

"Just asking the question can have an impact," he said. "It's almost as if we are equipped to express our suffering in different ways, through a variety of channels, and for some people, merely asking the question can open all the channels. And, of course, that affects the way pain can be measured."

In another experiment he asked volunteers to expose their arms and hands to extreme cold for as long as they could. Not only did he find that peoples' physical responses to the same pain stimulus differed. But as he reviewed videos of the experiment he noted significant differences in body language as well.

Pain is real, Dr. Sullivan said. There are significant differences in the way some people experience their pain and vast variations in the way they express it. As a psychologist, he finds the body language fascinating.

When a person has a headache, for example, they often rub their forehead. When asked why, they say the action soothes them "and that's okay," he said. But pain behaviour has a significant inter-personal component as well.

"It can be a signal," he said. "There are a lot of messages going out. Some have to do with the strength of the relationship – 'do you care?' Some have to do with the fear that it may get worse – 'I may need your help soon.' "

"But from my perspective, if certain psychological factors affect pain, then maybe targeting those factors can help people. I'm interested in defining how pain affects what people do. Perhaps, in some cases, we cannot reduce the suffering caused by pain beyond a certain point. But can we reduce the disability that is related to it?"

As a clinician, he said, helping people deal with their disability is a primary focus.

Dr. Sullivan has lectured nationally and internationally and written dozens of articles on the social and behavioural factors associated with pain and disability. His research has been aimed at developing ways to limit and prevent disability in people suffering from persistent pain. He works closely with therapists and work-place injury specialists.

"Often the best interventions are the simplest," he said. "For example, it is important to remain as active as possible."

Pain, he explained, is more than a physical sensation. It is also a behavioural and inter-personal phenomenon. And those are the aspects that he looks at most closely.

Pain can affect our lives in many different ways. At its most basic level there is the physical distress that pain brings and one can appreciate, he said, the great stress that comes with living every day of one's life with persistent high levels of pain.

But pain also has an effect on the different roles that life brings.

"One person may have several roles," he said. "They may be a parent, a friend, a spouse and a worker. Each role affects who we are and each is associated with different activities. Pain can interfere with these activities and the more that we discontinue them, the greater the erosion of the sense of who we are."

Research has shown that the more inactive the person becomes, the more physical pain they feel and the more isolated they become. "So we have to be as active as we can be. That's key."

Dr. Sullivan is looking forward to exploring this further at McGill. He plans to look more closely at what determines different forms of pain behaviour and develop ways of assessing it that can be used in routine clinical practice. The fact that he can share his interests with so many colleagues in pain research from so many fields was a major factor in his decision to come here.

MRI FACILITY:
PAIN IMAGING AT McGILL

Sometimes, finding the money for research isn't as big an issue as finding the space for it.

That certainly was the case with the new small animal magnetic resonance imaging (MRI) facility in the Genome building that was installed as a result of close cooperation between the McGill Centre for Research on Pain and the Montreal Neurological Institute.

"It took a little time but with real collaboration between the Brain Imaging Centre at the MNI and the Pain Centre, we were able to work something out," said Dr. Catherine Bushnell

Dr. Bushnell is the Harold Griffith Professor of Anesthesia and Professor in Dentistry and Neurology at McGill University. She is also the director of the McGill Pain Centre and Editor-in-Chief of IASP Press.

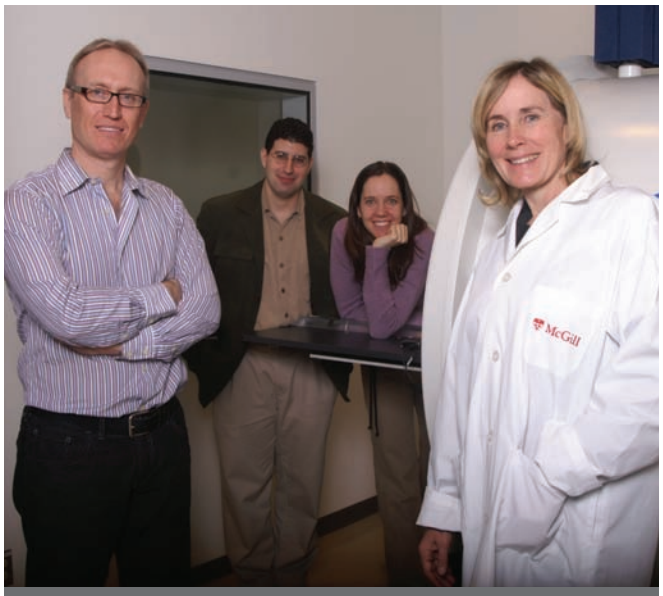
"There was $35-million in grants for a whole array of brain-imaging equipment and no place to put it at the 'Neuro,'" she said. But the pain people had space near their animal facility in the Genome building where there was a surgical area and behavioural testing space "so it was better for everybody for the small animal MRI to be located there."

But before it could be installed, nearly $300,000 in renovations had to be done to the building to accommodate the new machine and its quench-pipe system. This was paid for by the Pain Centre and the Louise Edwards Foundation "who were extremely generous with us," Dr. Bushnell said.

The equipment is state-of-the-art and the only facility of its kind in Montreal. It works like a human MRI except that everything is smaller and Dr. Barry Bedell of the MNI, for one, is delighted with it.

"It allows the non-invasive measurement of brains and other organs in live animals over a period of time," Dr. Bedell said.

Pain Centre investigators use animal models to discover the underlying mechanisms of pain. At the magnetic resonance imaging and neuro-imaging analysis lab in the Genome building, structural and functional imaging studies of



Dr. Bruce Pike, Director of the McConnell Brain Imaging Centre (BIC), Dr. Barry Bedell, Director of the Small Animal Imaging Laboratory (SAIL) at the BIC, which includes the fMRI facility, Dr. Simone Zehntner, the Assistant Director of SAIL, and Dr. Catherine Bushnell, the Director of the MCRP.

acute and chronic pain models are performed.

"Chronic pain, for example, develops over time," Dr. Bushnell explained. "When we examine animals over time, we can see why some develop chronic pain and others don't. And when we are dealing with living animals, it's easier to examine them in terms of active functions."

Dr. Bedell added, "Traditionally the way we have done it has been a static procedure. Now, for example, we can see the living brain actually responding."

He is assistant professor in the Department of Neurology and Neurosurgery in the Faculty of Medicine and Director of Small Animal Imaging at the MNI. And he is looking forward to working further with the Pain Centre.

In collaboration with Dr. Terry Coderre, a Pain Centre member and expert in animal behavioural testing, Dr. Bushnell plans to use the new equipment in her own work, specifically to study whether pain injures the brain.

"Recent studies in chronic pain patients suggest that experiencing pain for years can lead to a premature aging of the brain," she said. "With age, we lose cells in the brain, just as we lose muscle mass. There is now evidence that chronic pain increases this age-related "shrinking" of the brain.

"With our new magnetic resonance imaging equipment, we can look into the brains of rats from week to week, as they develop chronic pain after a nerve is injured. Pictures can be taken over and over again across a period of months or years.

"Since rats only live to be about three years old, their natural aging is much quicker than that of humans. Thus, in a period of a year, we can see changes in the brain that might take 15 or 20 years to occur in people after the same injury."

Dr. Theodore Price says the new facility "has the potential to completely change the way we think about doing experiments."

Dr. Price is a National Institutes of Health (USA) Fellow working at the McGill Centre for Research on Pain with Dr. Fernando Cervero, a world-renowned specialist on visceral pain.

"The small animal MRI gives us access to the entire brain at one time," Dr. Price said. "Normally we look at a single neuron, for example, or examine something that happened in the past. This is very significant. It means that we can study things in living context."

Dr. Cervero and Dr. Price plan to use the new facility in two different projects. One should lead to a greater understanding of increased visceral pain sensitivity in the central nervous system of post-menopausal women. The other will try to cast light on why some changes in pain sensitivity at the level of the spinal cord appear to be related to fragile x (FXS) mental retardation, the leading inherited form of mental retardation in humans.

Both studies should help our understanding of how pain sensitivity in the spinal cord affects the way the central nervous system processes pain.

The new facility "opens up a whole new way of doing things," Dr. Price said.

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