

RESEARCH
that is
transforming care

DISCOVER



AT CAMH, WE CARE, **DISCOVER**, BUILD AND SHARE TO TRANSFORM LIVES

Our Mission

Improving the lives of those affected by addiction and mental health problems and promoting the health of people in Ontario and beyond.

Our Vision

Strong and healthy communities, in which people with addiction and mental health problems can access appropriate and effective services and live as full participants.

Pictured on the front cover, from left to right:

Dr. Daniel Mueller – Head, Pharmacogenetics Research Clinic
Dr. Brendan Andrade – Clinician-Scientist, Child, Youth and Family Program
Dr. Lori Ross – Research Scientist, Health Systems & Health Equity Research Group
Dr. Sylvain Houle – Director, Research Imaging
Dr. James Cantor – Head, CAMH Law and Mental Health Research Section

Photographs by Rick Chard • rickchard@bmts.com

CAMH is a research and teaching hospital fully affiliated with the University of Toronto.

CAMH is a Pan American Health Organization / World Health Organization Collaborating Centre in Mental Health and Addiction.

A copy of the CAMH Annual Report, 2010–2011, *Building the Future*, is available at www.camh.net or from CAMH Public Affairs at public_affairs@camh.net

LETTER FROM THE VICE-PRESIDENT, RESEARCH



The Centre for Addiction and Mental Health (CAMH) is an internationally recognized academic health science centre with a reputation for innovative research. With more than 450 scientists, staff and trainees, our research enterprise is focused on transforming our understanding of mental illness and addictions, and improving outcomes for the one in five Canadians who will encounter mental health problems in their lifetime.

An interdisciplinary approach—and access to a large patient population—helps define the CAMH advantage. Today's talented researchers are putting advanced technologies to work across disciplines to yield valuable insights and new treatment and prevention opportunities. And it's paying off: in a highly competitive field, CAMH researchers are increasingly successful in drawing in external funding from major granting agencies in Canada and the U.S.

It's truly an exciting time to be conducting research at CAMH. We are in the midst of our Research Renaissance Project, the largest-ever scientific endeavour at CAMH, which is reinvigorating our already successful research program.

This project, spurred by major investments into our infrastructure, saw some key milestones over the past year. We have acquired a new MRI and cyclotron, as well as new genetic sequencing and genotyping technologies, which will enhance our capacity to do brain imaging and genetics research.

CAMH's mobile research laboratory, the first of its kind in Canada, is now set up to do research in the community of Port Colborne.

These enhancements are enabling our researchers to unravel the complex causes of mental health and addiction disorders, and to find effective prevention and treatment approaches. We are grateful to the Canada Foundation for Innovation, the CAMH Foundation and Ontario's Ministry of Research and Innovation for their support.

Our scientists had another productive year. This year, they identified a brain protein peptide that is a new target for treating depression, a gene that contributes to autism, and a new technique to identify healthy individuals at risk for late-onset Alzheimer's disease. They showed that mindfulness meditation may be just as effective as medication in preventing the relapse of some types of depression. They began the only clinical trial outside of the U.S. on the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders*. And they mentored 140 trainees. The list of prestigious awards and successful grants won by emerging and established CAMH scientists continues to grow.

Without the dedication of our scientists, research staff, postdoctoral fellows and volunteers, these accomplishments would not have been possible. As the momentum from the Research Renaissance Project continues to inspire us, the coming year holds even more promise than the last.

Sincerely,

A handwritten signature in black ink, appearing to read 'Bruce Pollock', written in a cursive style.

Dr. Bruce G. Pollock, Vice-President, Research

DISCOVER

CAMH is uniquely positioned to make discoveries that benefit people with mental health and addiction problems.

“From neuron to neighbourhood,” our integrative approach to research encompasses genetics, molecular neuroscience and brain imaging, clinical and community-based studies, and epidemiological, social and policy research. Our research has a common goal—to improve the lives of people with mental illness and addictions.

Six CAMH scientists hold Canada Research Chairs.

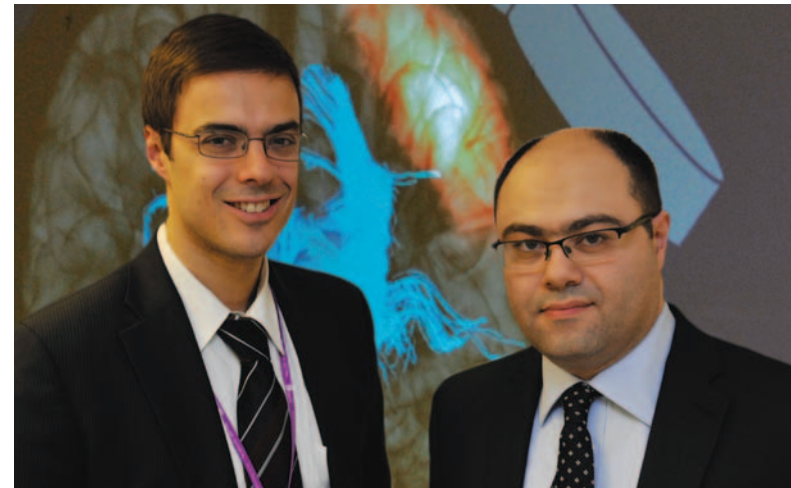
Through our Research Renaissance Project, CAMH’s largest-ever scientific endeavour, our capacity to leverage this integrative approach will grow in the coming years. This investment into research infrastructure has provided the momentum to unravel causes, and discover effective prevention and treatment approaches.



Mental illness in later life

CAMH has a strong research program focused on aging and mental health. Over the past year, our scientists have made discoveries in both prevention and treatment. In prevention, Dr. **Aristotle Voineskos** used an innovative combination of brain imaging and genetic analysis to identify healthy people at risk for late-onset Alzheimer’s disease. He identified a genetic variation of a protein that may play a role in Alzheimer’s. The protein, brain-derived neurotrophic factor, is essential for learning and memory functions. “Early identification is key, because in addition to seeking therapeutic treatments early to reduce suffering, delaying Alzheimer’s onset by only two years has the potential of saving the Canadian health care system nearly \$15 billion over the next 10 years,” says Dr. Voineskos.

Drs. Aristotle Voineskos (l) and Tarek Rajji in front of an image of a transcranial magnetic stimulation coil applied to the brain.



More than half of people with Alzheimer's disease experience distressing symptoms such as delusions, hallucinations or agitation, and they are often treated with antipsychotic drugs such as risperidone. This drug breaks down in the body into a product called 9-hydroxy risperidone. A study by Drs. **Bruce G. Pollock** and **Robert Bies** found that high concentrations of the drug's by-product led to people quitting their medication because it was not working or because of side-effects. Dr. Pollock is currently co-leading a multi-site study of a potential alternative treatment, supported by the U.S. National Institute on Aging and National Institute of Mental Health.

A number of mental illnesses are associated with problems with memory, attention and planning, and other cognitive deficits. The presence of these deficits can predict how well people function in their daily lives. But the way these deficits affect older adults in the community is unclear.

Drs. **Benoit Mulsant** and **Tarek Rajji** are studying cognitive changes in older adults with bipolar disorder and schizophrenia, respectively. Both are evaluating a program that provides social skills and cognitive-behavioural group therapy for adults with schizophrenia to prevent hospitalization and enable them to continue living in the community.

About 14 per cent of people who take medication to treat Parkinson's disease develop impulse control disorders, such as gambling. Dr. **Antonio Strafella** has used PET imaging to show that these Parkinson medications, which stimulate dopamine receptors in the brain, can interfere with the areas of the brain involved with reward and impulse control—areas connected to addictive behaviours. In his study of people with gambling problems, these brain regions were less activated than those of people who did not have problems. "This finding could help identify anti-parkinsonian medications that do not interfere with those brain regions in patients who are vulnerable to developing impulse control disorders," he says.

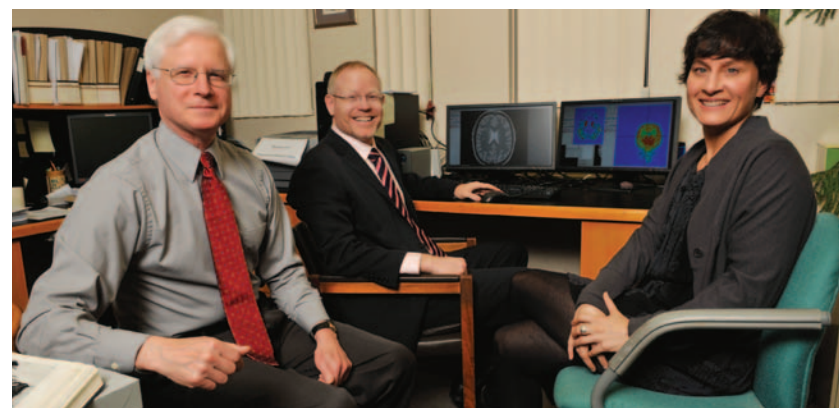
CAMH has also been involved in the development of the **Toronto Dementia Research Alliance** along with the University Health Network (UHN), Sunnybrook Health Sciences Centre, Baycrest, St. Michael's Hospital and the University of Toronto.

Addictions: From laboratory to community

Addiction researchers at CAMH are applying findings from genetic and brain research to the discovery of effective clinical treatments. They also identify the changing trends in substance use and their effects on individuals and communities, which provide direction for additional research, treatment and policy.

Drs. **Rachel Tyndale** and **Tony George** are looking at smokers' genetic responses to smoking cessation medications, in order to improve outcomes. A genetic biomarker known as the nicotine metabolic ratio—previously identified by Dr. Tyndale—can predict whether someone breaks down nicotine quickly or slowly. A randomized, controlled multi-site study is underway that will use the biomarker to predict the success of three approaches: a nicotine patch, the drug varenicline and a placebo.

The drug ecstasy (MDMA) is used by about one in 20 students in grades 11 and 12, according to CAMH's 2009 Ontario Student Drug Use and Health (OSDUHS) survey. After 12 years of contradictory studies, CAMH brain imaging research has confirmed that this stimulant has potentially harmful effects. Drs. **Stephen Kish** and **Isabelle Boileau** have shown that levels of a



Drs. Stephen Kish (l), Russell Callaghan and Isabelle Boileau work together to investigate the impact of substance use, using brain imaging and epidemiology.

protein called serotonin transporter (SERT) are low in the neural tissue surrounding the main part of the brain of ecstasy users. Ecstasy interacts with SERT, leading to the release of serotonin, which is important for controlling moods and impulses. This finding helps explain why users need to keep taking higher doses to get the same effects. “The need for higher doses might well increase the risk of harm,” says Dr. Kish.

Tobacco experts point to the dramatic reduction in teen smoking, due to taxes and restricted cigarette sales, as a success story. However, Dr. **Russell Callaghan** showed that contraband cigarettes now account for 43 per cent of all cigarettes consumed by Ontario students in grades 9 to 12 who smoked daily. Contraband cigarette prices are lower and there are no purchase restrictions, making cigarette access easier. Dr. Callaghan drew data from CAMH’s 2009 OSDUHS for this study.

CAMH has the largest single collection of DNA
from psychiatric patients in the world,
with about 23,000 DNA sets for 20 different illnesses.

Research breakthroughs in depression

Although standard treatments with medication and counselling are effective for many people with depression, they do not work for everyone, and side-effects can limit their use. Even if a treatment works initially, it may not work again if the depression recurs. CAMH scientists are exploring ways to prevent depression, seeking alternative targets for treatment, and addressing issues of treatment resistance and recurrence.



Dr. Fang Liu in her laboratory.

Dr. **Fang Liu** has developed a new protein peptide that offers the promise of a better treatment target for depression. First, she found that two brain receptors had higher levels of “coupling” or binding among people with major depression.

Next, she discovered

a way to disrupt this coupling using the new peptide. In the past, treatment relied on medications that mostly blocked serotonin or norepinephrine transporters. Her research may lead to an alternative approach to managing this problem.

Another option for people with depression is meditation. Mindfulness-based cognitive therapy using meditation is just as effective at preventing relapse as medication, according to a study by Dr. **Zindel Segal**. “Mindfulness-based cognitive therapy is a non-pharmacological approach that teaches skills in emotion regulation so that patients can monitor possible relapse triggers as well as adopt lifestyle changes conducive to sustaining mood balance,” says Dr. Segal. His ongoing research is looking at the effects of this approach on the brain through neuroimaging.

Building upon his research that found a chemical explanation for why new mothers are at risk of developing postpartum blues and depression, Dr. **Jeff Meyer** is now working to develop a preventive approach. Using PET imaging, his earlier research showed that a brain protein called monoamine oxidase A (MAO-A) is higher among people who have depression; more recently he discovered MAO-A levels are also higher among women who have very recently given birth. His team is examining whether a dietary supplement can provide nutrients removed by high levels of MAO-A, and thereby lower the risk of postpartum depression.

Where you live: Community and workplace research

Community-based research helps to show how specific mental health and addiction issues play out in different settings. CAMH's new state-of-the-art mobile research lab—the first in Canada dedicated to mental health and addictions—enables our scientists to do research in underserved communities across Ontario. The lab is equipped with a satellite to send data, interview rooms and a lab to store saliva or hair samples for genetic testing. Dr. **Samantha Wells** is leading research funded by the Canadian Institutes of Health Research (CIHR) in the lab. This includes studies on stress, the health care experience of people with concurrent disorders, and intimate partner violence.



*CAMH scientists (l-r)
Drs. Rachel Tyndale, James
Kennedy, Bruce G. Pollock
(VP of Research), Jürgen Rehm
(obscured), Benoit Mulsant
(physician-in-chief) and
Samantha Wells in front of the
mobile research laboratory.*

Chronic stress can lead to burnout and worsen existing mental health problems or physical disabilities. This is why understanding work-related stress is important. A study by Dr. **Carolyn Dewa** indicates that workers most invested in their jobs have the highest stress levels. In a survey of 2,737 workers, 18 per cent reported that their job was “highly stressful.” The odds of reporting high stress were greater if workers were managers or professionals, if they thought their poor job performance could negatively affect others, or if they worked long or variable hours. The importance of this area of research is becoming increasingly recognized by major corporations and industries.



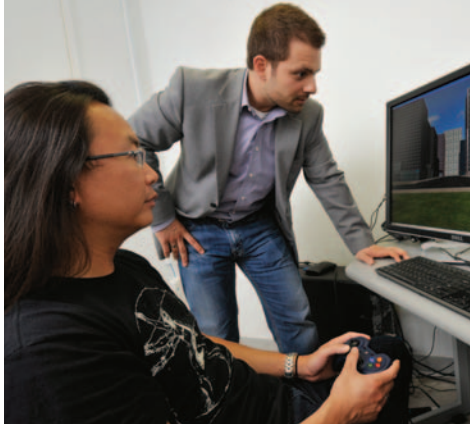
CAMH scientist Dr. Carolyn Dewa (l) being interviewed on CP24 about her research findings on workplace mental health.

About 29,000 Ontario students in grades 7 to 12 are gambling problematically, according to a study led by Dr. **Robert Mann**, which was based on the Ontario Youth Gambling Report. The students with problem gambling indicators also reported higher rates of psychological distress, alcohol and/or other drug use, and suicide attempts.

New schizophrenia research

CAMH's scientists are using novel techniques and assessment tools in schizophrenia research. These include virtual reality, genetic testing to guide medication prescription, and repetitive transcranial magnetic stimulation (rTMS) as a medication alternative.

Drs. **George Foussias**, **Gary Remington** and **Albert Wong** will be using virtual reality to investigate motivation and spatial navigation in people with schizophrenia. For instance, in a new study, participants will be prompted to complete everyday tasks, such as doing their laundry or shopping for groceries, in a simulated city. One goal is to develop a more objective way of measuring motivation than traditional self-reported questionnaires, using participants' active engagement in the virtual environment to complete these tasks. Dr. Foussias envisions that this tool could aid clinicians in treatment planning. The researchers will also use functional magnetic resonance imaging (fMRI) to correlate motivation with brain functioning when completing tasks.



Drs. George Foussias (r) and Albert Wong in front of a simulated virtual reality city for schizophrenia research.

Dr. **Sean Kidd** is conducting a pilot study of a “real-world” application of an intervention called Cognitive Adaptation Training (CAT). CAT addresses the memory, attention or problem-solving deficits that may challenge a person with schizophrenia from getting dressed and out the door to a job or school. Using CAT, a specialist assesses each client and determines an individual protocol, which could involve packaging clothes for each day of the week, and setting up voice alarms with encouraging words or reminders to take transit passes. CAT has led to improvements in a range of areas, including employment, but the gains do not last after the study program ends. This pilot study, conducted with the University of Texas, will examine an application in which case managers will maintain CAT indefinitely in consultation with CAT specialists.

CAMH scientists published almost 450 articles in peer-reviewed journals this year. More than a third of these articles were in “high impact” journals.

In 2010, CAMH was the only field trial site in Canada selected to help assess the clinical use of the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-V). The American Psychiatric Association's DSM is used in many parts of the world to help diagnose mental illness. The trials are being led by Drs. **Bruce G. Pollock**, **Michael Bagby** and **Kwame McKenzie** in personality disorders, schizophrenia, schizoaffective disorder and attenuated psychotic symptoms syndrome, a proposed new DSM item that refers to people who may be at high risk of developing schizophrenia.

CAMH has the only clinic in North America connected with neuroimaging facilities for people at high risk of developing schizophrenia because they have shown some mild symptoms. Using PET imaging, Dr. **Romina Mizrahi** has demonstrated that people who are at high risk experience a large release of the chemical dopamine when stressed. The dopamine release is at levels slightly lower than levels of people with schizophrenia, but higher than that of people without any symptoms. Dr. Mizrahi's research points to a way to diagnose and prevent the development of schizophrenia among people at high risk, by modulating their dopamine-stress response.



Dr. Romina Mizrahi with a PET machine dedicated to mental health and addictions research at CAMH.

Last year, CAMH discoveries yielded nine patents for epigenetic discoveries and technologies, pharmacogenetics and new antipsychotic compounds.

Genetics, epigenetics and mental health

In the expanding field of pharmacogenetics, scientists are testing genes that predict which drugs will produce the best response with the fewest side-effects. Other CAMH researchers are identifying genes that cause mental illness or neurological disorders, and exploring how the environment works at the DNA level to produce disease. Our scientists are also using brain imaging to relate genetic information to brain structure and function.

Drs. **James Kennedy** and **Daniel Mueller** conduct research on liver gene enzymes, which can identify which patients will break down antipsychotic or antidepressant drugs quickly or slowly. This type of testing can predict how well someone will respond to a medication and the risk of side-effects. Dr. Kennedy will be studying the effectiveness of having family doctors—who prescribe about 80 per cent of these drugs—use tests to provide the best treatment to their patients. If successful, this approach could be adopted widely to greatly reduce the burden of these side-effects.

Dr. **John Vincent** has shown why autism spectrum disorder may affect four times as many males than females. In a study with the Hospital for Sick Children, the researchers found mutations on a gene on the single X chromosome that males carry. This mutation may disrupt crucial processes during brain development, contributing to the occurrence of autism.

Dr. **Arturas Petronis** is continuing his groundbreaking research on epigenetics—an area of molecular biology that explains how environmental factors, such as stress or nutrition, influence what genes do. “We are describing at the molecular level how environmental factors may trigger our inherited risk factors for genetically based diseases,” says Dr. Petronis. His team is in the midst of a major project to scan the entire human genome for epigenetic differences specific to bipolar disorder. The study is supported by a grant from the U.S. National Institutes of Health.

DISCOVER award highlights

The Brain and Behavior Research Fund (NARSAD) gave Young Investigator Awards to six CAMH scientists: Drs. **Daniel Blumberger**, **George Foussias**, **Romina Mizrahi**, **Tarek Rajji**, **Arun Tiwari** and **Aristotle Voineskos**.

Drs. **Vincenzo De Luca** and **George Foussias** were awarded American Psychiatric Association/AstraZeneca Young Minds in Psychiatry Awards.

Drug Policy and the Public Good won first prize in the public health category of the British Medical Book Awards, thanks in part to contributing CAMH authors Drs. **Benedikt Fischer** and **Jürgen Rehm**.

Dr. **Jeff Daskalakis** won the Young Investigator Award from the Canadian College of Neuropsychopharmacology.

The Kaiser Award for Excellence in Leadership was presented to Dr. **Patricia Erickson** in recognition of her outstanding contribution to promoting the philosophy and policy of harm reduction in Canada.

Dr. **Jeffrey Meyer** was awarded the Society of Biological Psychiatry's prestigious A.E. Bennett Award for major discoveries in brain chemistry using PET imaging, over the last decade.

Dr. **Daniel Mueller** received an Early Researcher Award from Ontario's Ministry of Research and Innovation, as part of a program to help attract and retain the best and brightest research talent.

The American College of Psychiatrists honoured CAMH's vice-president of Research Dr. **Bruce G. Pollock** with its 2011 Award for Research in Geriatric Psychiatry.

Dr. **Rachel Tyndale** won the Heinz Lehmann Award from the Canadian College of Neuropsychopharmacology and the Langley Award from the International Society for Research on Nicotine and Tobacco.

Dr. **Aristotle Voineskos** was awarded the 2011 Siminovitch-Salter Award, presented to an outstanding PhD graduate of the Institute of Medical Sciences (IMS) at the University of Toronto.

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