



iscovery

Across the lifespan.
2013–2014 CAMH Research Annual Report

Our

Vision

Transforming lives through research.










Our

Commitment

Our discoveries and innovations will lead to a better quality of life for the people and communities we serve, and beyond.



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Letter from the
VP
of Research



CAMH continues to transform the way that mental illness and addictions are understood and treated. Research is a crucial part of this charge.

Over the past year, we have moved forward in a number of directions through external partnerships and internal initiatives.

We have established partnerships with the U.S. biotechnology company Assurex Health to advance personalized medicine, and with the Institute for Clinical Evaluative Sciences (ICES) to improve mental health and addiction services across the province.

Within CAMH, we continue to build upon our scientific expertise. We have recruited two international experts—our inaugural Campbell Family Chair in Clinical Neuroscience, who is an expert in depression and aging, and a specialist in magnetic resonance spectroscopy techniques to expand our brain imaging capabilities. You can learn more about their work within this report.

We continue to work with our Toronto hospital colleagues to develop a cross-organizational approach on research and treatment for women, and for children and youth. CAMH's new chief of General Psychiatry holds a joint appointment with Women's College Hospital, bringing greater focus at CAMH to trauma-informed research on women. This follows the joint appointment, last year, of the new chief of the Child and Youth Mental Health Collaborative at CAMH, the Hospital for Sick Children and the University of Toronto.

Finally, it is worth noting the important work that occurs behind the scenes. We have undertaken major initiatives to improve research quality and compliance, to develop a new bioinformatics strategy and to advance our commercialization activities. This work is essential in supporting our ongoing success, which is reflected in the stories presented in this year's report.

Bruce G. Pollock, MD, PhD, FRCPC

Vice President, Research
Director, Campbell Family Mental Health Research Institute



Partnerships & News CAMH Research

First Campbell Family Research Symposium

The inaugural Campbell Family Mental Health Research Symposium featured North American thought leaders in mental health research: Dr. Thomas Insel of the U.S. National Institute of Mental Health, Dr. Daniel Weinberger of the Lieber Institute and Dr. Anthony Phillips of the Canadian Institutes of Health Research. CAMH scientists presented on topics such as epigenetic drugs as treatment for mental illness, and treatment biomarkers for brain stimulation in depression, among others.

Commercialization update

Seven U.S. patents were issued for CAMH inventions in the past year. The patents were related to treatments for depression, addiction, schizophrenia, and stroke or epilepsy; for genetic mutations to screen for muscular myopathy and Joubert syndrome; and for a method to diagnose mood disorders. In addition, two other discoveries were licensed to AssureRx Canada, for genetic markers predicting suicide risk and antipsychotic-induced weight gain.



Partnerships & News

continued

▲ New brain imaging capabilities

Dr. Napapon Sailasuta, an expert in developing magnetic resonance spectroscopy (MRS) techniques, has been recruited to CAMH's Research Imaging Centre from Huntington Medical Research Institutes in California. Her expertise will expand MRI capabilities at CAMH. MRS provides biochemical information about brain tissues and chemical processes.

Improving service delivery

Dr. Paul Kurdyak is leading the new Mental Health and Addictions Research Program at the Institute for Clinical Evaluative Sciences (ICES), aimed at improving inequities in mental health and addiction service delivery in Ontario.



▲ CAMH hosted a CIHR Café Scientifique on brain plasticity and mental illness with (l-r) CAMH scientists Dr. Albert Wong and Dr. Tarek Rajji.

▲ Larry Meikle describes his experience with personalized medicine.

Global report on alcohol

As part of CAMH's role as a World Health Organization Collaborating Centre, Dr. Jürgen Rehm and his team contributed to the 2014 *Global Status Report on Alcohol and Health*. The WHO report provides a snapshot of alcohol consumption and the impact of public health and policy responses in 194 member states.

[!\[\]\(8d0f0e0fe25b320c33272c52aec1fbca_img.jpg\) Global Status Report on Alcohol and Health](#)

▲ Advancing personalized medicine

CAMH announced a partnership with U.S. biotechnology company Assurex Health to advance the use of personalized medicine—genetic testing to determine a person's response to psychiatric medications, avoiding treatment failure and side-effects. AssureRx Canada was established as a subsidiary of the U.S. company, with its Canadian office and laboratory on CAMH premises.

[!\[\]\(3cb60d42b10e53f9522bb0b392c1c4cd_img.jpg\) Assurex CAMH partnership video](#)

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Our discoveries and innovations will lead to a better quality of life for the people and communities we serve, and beyond.

Research

Pillars

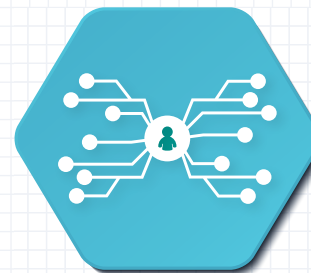
At CAMH, we describe our research on mental illness and addiction according to three pillars:



**Brain
science**



**Clinical
research**



**Social &
epidemiological**

Each pillar addresses an important aspect of mental illness and addiction. A better understanding of brain structure and function can help reveal causes of illness and new targets for treatments. By conducting innovative clinical research, we can positively impact care. In identifying the complex social factors that contribute to illnesses, we can inform system-level interventions and public policy.

For an individual with an illness, the research undertaken in each pillar is relevant throughout their lives. The roots of illness may begin even before birth. Experiences during infancy and childhood can influence the development of mental health and substance use problems later. Symptoms can be treated and recur in different ways. Some mental illnesses can emerge late in life. For this reason, scientists are increasingly working across these pillars, and combining their scientific expertise, to better understand these complex, chronic conditions. This year, we show how the contributions from each pillar provide pieces of evidence about mental illnesses and addictions across the lifespan.

See how our research is helping to transform lives across the lifespan.



Pregnancy

Antidepressants in pregnancy: Outcomes and risks

Many pregnant women don't take antidepressants for fear of exposing their unborn child to potential health risks.

To provide some guidance on this issue, **Dr. Lori Ross** and colleagues conducted a series of meta-analyses that pooled study results of antidepressant use during pregnancy. They looked at potential consequences of antidepressant use for the baby, including birth defects and neonatal adaptation syndrome—temporary brain-related symptoms such as insomnia, agitation or poor feeding—and considered the effects of untreated depression on the mother.

As reported in *JAMA Psychiatry* and the *Journal of Clinical Psychiatry*, the authors' findings confirmed that infants who had been exposed to antidepressants before birth had a higher risk of neonatal adaptation syndrome, respiratory distress, tremors and cardiovascular birth defects. However, the newborns were

also exposed to risks if their mother's depression went untreated: mothers were less likely to initiate breastfeeding and were more likely to deliver prematurely.

Ultimately, the risks of medication use have to be weighed against the effects of depression. "Deciding on the appropriate approach to medication use during pregnancy can be a challenge, for both mothers and doctors," says Dr. Ross. "We hope physicians will use this research to provide expectant mothers with the best available evidence to inform this decision."

According to the World Health Organization, depression is one of the leading causes of death and disability among women aged 18 to 44 years.

[!\[\]\(ceb7cef9f9d693d102dfe501130037c6_img.jpg\) JAMA Psychiatry article](#)

[!\[\]\(8a8ea273bba45b658cf4779d37ab61e8_img.jpg\) Journal of Clinical Psychiatry article](#)



Dr. Karen

Urbanoski

Scientist

Dr. Karen Urbanoski and colleagues are evaluating the impact of integrated treatments for pregnant women and new mothers with substance use problems. Integrated programs, which combine addiction treatment with prenatal and medical care and other services, were developed to support women who are underserved. The study is supported by the Canadian Institutes of Health Research and the Ontario Ministry of Health and Long-Term Care.

Infancy

Understanding babies' stress response

The way a mother responds to her baby's coos and cries is a crucial part of a child's overall development. How attuned she is to her baby's signals—her maternal sensitivity—appears to affect the baby's stress response system.

A collaborative study with **Dr. Robert Levitan** and Ryerson University colleagues, headed by **Dr. Leslie Atkinson**, clarified this link between maternal sensitivity and a child's stress response in a set of experiments reported in *Psychoneuroendocrinology*.

In one experiment, 17 month-old babies experienced the stranger test, in which they were left with a female stranger or alone in a child-friendly room at different times. The babies' levels of cortisol, a stress-induced hormone, were tested before and after each experiment in the lab. Maternal sensitivity had been measured earlier, at home.

Normally, cortisol will rise temporarily in response to a threat, as it provides a burst of energy and mental focus. This was shown in the stranger test—but only in babies with sensitive mothers.

In contrast, babies of mothers with lower sensitivity didn't show this fluctuation. This finding suggests that maternal sensitivity helps children develop a normal cortisol stress response, which will provide protection against later stresses, potentially across the lifespan.

"Another interesting finding was that the correlation between a mother's and her child's cortisol levels was much higher when mothers were sensitive," says Dr. Levitan. "This suggests that emotional and hormonal attunement occur together in these particular families."

[!\[\]\(eaac180de418db4eae4b4cefebda75e8_img.jpg\) *Psychoneuroendocrinology* article](#)

Childhood

Childhood foster care and mental health risks

Indigenous children in Canada continue to be over-represented in foster care relative to non-Indigenous children. The long-term mental health effects of foster care placement are not well known.

In a study published in *Psychiatry Research*, **Dr. Violet Kaspar** found that major depressive episodes and thoughts of suicide occurred at significantly higher levels among Indigenous people with histories of residing in foster care.

According to Dr. Kaspar, foster care placement yields inequalities in cultural, psychosocial, economic and community-level mental health determinants that may explain, in part, the emergence of depression and suicidal thoughts in Indigenous populations.

Using data on a national sample of 7,534 Métis people, she found that respondents who were placed in care reported lower cultural attachment, spirituality, self-esteem, community resilience and socioeconomic status during the intervening years relative to the non-fostered group. These factors, in turn, explained the depression and suicidal ideation.

[!\[\]\(c2b822cc4b4175583c9e9f364bcce273_img.jpg\) *Psychiatry Research* article](#)



Treating childhood disruptive behaviours

For a concerning number of children with disruptive or aggressive behaviour, existing treatments are ineffective. This may be because underlying psychological issues that contribute to their disruptive behaviour—such as anxiety or aspects of their temperament—aren't being effectively addressed.

To improve outcomes among these children, **Dr. Brendan Andrade** and his team conducted a three-year clinical trial called the ABATE (Addressing Behaviour and Treatment Effectiveness) project.

“We want to treat behaviour issues by targeting the underlying problem,” says Dr. Andrade. Using a randomized study design, the researchers compared two therapeutic approaches aimed at developing social, coping and emotional regulation skills: a group-based program, in which children worked with their parents, and individualized parent-child treatments. Their goal was to identify effective therapies, as well as characteristics of children and parents that affected treatment success for each approach.

Early results show that both treatments reduced disruptive behaviour, but effectiveness depended on whether there was an underlying condition. For example, for children with anxiety in addition to conduct problems, the group-based therapy was not as effective, suggesting that underlying conditions do need to be considered.

“We applied these therapies to a diverse range of kids coming into treatment at CAMH, so our results likely apply to other clinical settings,” notes Dr. Andrade. “Most randomized controlled trials are selective about who is included, so findings often cannot be generalized.”

Disruptive behaviour in childhood predicts future addiction, mood and anxiety disorders, so intervening early holds promise for prevention. Next, the ABATE team aims to conduct a larger study, involving other children's mental health centres, using neuropsychological measures to examine changes in brain function in children with treatment.

 **ABATE Project**

Q&A

Meet Our Experts



LEAD

CAMH foundation is deep
individuals



Valerie Taylor

In 2014, Dr. Valerie Taylor was appointed chief of General and Health System Psychiatry at CAMH, in a cross-collaborative role with Women's College Hospital (WCH), where she is the psychiatrist-in-chief. Dr. Taylor brings expertise in the areas of obesity, chronic physical illness and mental health, with a focus on the developmental origins of illness, particularly the effects of the in utero environment. Her dual role will enhance women's mental health care from both clinical and health systems perspectives.

Q. What drew you to researching the links between physical and mental health?

A. During my psychiatry residency at McMaster University, I became interested in understanding why I was seeing so many patients on the inpatient unit with diabetes, cardiovascular disease and other illnesses that really affected their psychiatric care. Dr. Arya Sharma had just been recruited to be Canada's first obesity research chair, and I asked if he would help me create a research program on the relationship between mental health and metabolic-related diseases. It ended up being the first multidisciplinary metabolic clinic in Canada.

I was particularly interested in understanding individual vulnerabilities to co-occurring psychiatric and medical problems; for example, which issue comes first, the weight or the depression? Trying to answer that question meant going back in time—all the way to pregnancy, hence my interest in women's health. Ultimately, mental health is married to physical health, and both should be studied and treated concurrently.

Q. What are your priorities in your dual role?

A. I'm very interested in health systems and how people move through the system, especially with respect to medical psychiatry. Understanding the different pieces—hospital networks, family practice, community care, other partners—and how they work together is a huge focus, because streamlining care is very important. For me, another key aspect of this role is mentorship. I'd like to ensure support for researchers, and all staff, at CAMH and at WHC.

Q. What is your current research focus?

A. We're working on an entirely new area of study, which is whether or not psychiatric illnesses such as major depressive disorder (MDD) are associated with certain bacteria in the gut. We're examining changes in these bacteria before and after treatment with antidepressants, and exploring whether there are differences in gut bacteria between people with and without depression.

Gut bacteria is affected by nutrition and appetite, so we're asking our study participants to track their diets in detail. How diet affects health and disease is substantially under-researched. The aim is to answer key questions regarding microbial factors that contribute to mental illness. Understanding these links could be extremely beneficial for both prevention and treatment.

Q. What are some benefits of this cross-collaborative position?

A. WCH and CAMH have some complementary programs and a shared expertise. It's a perfect combination, particularly when dealing with mental illnesses that by nature involve myriad factors and comorbidities.

So far, as a partnership, CAMH and WCH have developed a transitional program between inpatient and outpatient care called P-STEP (Psychiatric Structured Treatment and Evaluation Program) to ensure that when people leave hospital care, all the medical pieces that sometimes get missed are taken care of; for example, managing medications or organizing home care. We're also piloting an evaluation scale to see if we can predict higher rates of hospital readmission among inpatients. If the scale can be validated, it will be a huge asset that we can export to the community. These projects really marry the competencies of both organizations.

Adolescence

Traumatic brain injuries linked to mental health problems

Traumatic brain injuries (TBIs) such as concussion are all too common in youth. But what does that mean for mental health? A study with St. Michael's Hospital, using data from the **Ontario Student Drug Use and Health Survey (OSDUHS)**, shows that teenagers who have suffered a TBI may be two to three times more likely than their non-injured peers to attempt suicide, be bullied or engage in high-risk behaviours such as selling drugs, carrying weapons, stealing or damaging property.

As reported in *PLOS ONE*, they are also more likely to become bullies, to seek counselling or to be prescribed medication for anxiety, depression or both. TBI refers to a head injury that caused either five minutes' loss of consciousness or overnight hospitalization.

As many as 20 per cent of adolescents in Ontario say they have experienced a traumatic brain injury, according to an earlier report the team published in the *Journal of the American Medical Association*.

"The relationship between TBI and mental health issues is concerning," says **Dr. Robert Mann**, who leads the OSDUHS.

The study provides the first population-based evidence showing the extent of the association between TBI and poor mental health outcomes among adolescents. The OSDUHS, developed by CAMH, is one of the longest ongoing school surveys in the world, with almost 9,000 student respondents between grades 7 and 12 in publicly funded schools across Ontario.

[Journal of the American Medical Association article](#)

[PLOS ONE article](#)

[Ontario Student Drug Use and Health Survey](#)

A new target for schizophrenia?

Physicians cannot yet predict whether teenagers and others at high risk of developing schizophrenia will go on to develop the illness. **Dr. Ariel Graff** is working to change that through his research on glutamate, an important neurotransmitter in the brain.

"High risk" means people have shown some behaviour symptoms, but have not yet had an episode of psychosis. Among those who have experienced psychosis, glutamate levels have been shown to be higher in certain regions of the brain.

Dr. Graff and colleagues examined whether glutamate levels changed after treatment. Using a brain imaging technique called proton magnetic resonance spectroscopy, patients who had experienced a psychotic episode were scanned before and four weeks after treatment with antipsychotic medications. The study, published in *JAMA Psychiatry*, confirmed that they had higher glutamate levels before treatment in certain parts of the brain.

More importantly, as patients' clinical symptoms decreased with treatment, so did glutamate levels. This suggests that glutamate is related to the illness—and therefore may be able to predict which high-risk teenagers will develop psychosis.

"This is an unexplored area," explains Dr. Graff. "Checking for elevated levels of glutamate in high-risk patients may help predict whether they will develop full-onset schizophrenia." Targeting glutamate might also provide a new avenue for treatment, given that current antipsychotic medications, which block dopamine activity, do not work in many patients.

[JAMA Psychiatry article](#)

Adulthood

Pathways to violence, beginning in childhood

People who repeatedly engage in violent offending typically have a history of problem behaviours stemming back to childhood, such as impulsivity, aggression and conduct problems. A small subset will also have psychopathy, a condition characterized by problems experiencing remorse or empathy. For these individuals, rehabilitation programs often fail.

Studies show childhood physical abuse is very common among men who grow up to exhibit psychopathy and engage in violent behaviour. Could there be a biological reason why?

Dr. Nathan Kolla is using imaging to look at brain structures of people involved in persistent aggressive behaviour who have been affected by childhood mistreatment.

“If we see differences in the brains of people who engage in repeated violence, and can show that these changes may relate to effects of childhood maltreatment, it provides the possibility to better understand the pathways leading to violence in these individuals,” he says.

Preliminary research findings, published in *Psychiatric Research: Neuroimaging*, show that some of the structural irregularities that distinguish violent offenders with psychopathy from those without, may indeed result from physical abuse in childhood.

While most children outgrow conduct problems and lead healthy productive lives, Dr. Kolla and his colleagues want to target the small subset who continue to offend into adulthood, to try to identify which children need help from the outset.

[!\[\]\(0b0636dbae614f97346d733ac650473d_img.jpg\) *Psychiatric Research: Neuroimaging* article](#)

Brain chemistry of pathological gamblers

Brain chemicals are known to be affected when a person is addicted to drugs. But what happens with behavioural addictions such as gambling, which involve a process rather than a substance?

Drs. Isabelle Boileau and **Martin Zack** have used cutting-edge positron emission tomography (PET) imaging to scan the brains of pathological gamblers, who can't control their urge to gamble despite harm to themselves and others. Their cravings or impulses are comparable to those of people with a drug addiction.

Despite some overlapping clinical features, the underlying brain chemistry appears to be different between pathological gambling and substance addictions, according to their study in *Molecular Psychiatry*. The differences relate to dopamine, a neurotransmitter in the brain, as well as the dopamine receptors to which it attaches to trigger cell activity. Dopamine receptor levels appear to be normal in gambling, relative to drug addiction. However, researchers found greater release of dopamine in pathological gamblers. This was related to the severity of their gambling and to a particular receptor, the D3 receptor.

Their results support the idea that brain mechanisms related to D3 receptors might contribute to pathological gambling. For this reason, potential treatment may include drugs blocking dopamine D3 receptors.

Pathological gambling has recently been added to the 5th edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) alongside other addictions.

[!\[\]\(ce2ec3be86913388b376b7085a0aa5b2_img.jpg\) *Molecular Psychiatry* article](#)

Easing the transition from hospital to community

There's a proven way to ease the transition for hospitalized clients as they move back to the community. The transitional discharge model (TDM), which focuses on therapeutic relationships, has shown benefits such as reducing clients' length of stay and readmission rates.

Yet TDM is not widely used. To help move this evidence-based practice into use, CAMH is participating in an implementation study addressing barriers to its uptake. The project is part of the Council of Academic Hospitals of Ontario's (CAHO) initiative, Adopting Research to Improve Care (ARTIC).

"The premise of TDM is powerful, with its emphasis on the therapeutic relationship. It is also unique as it provides a way to span the boundaries of inpatient to outpatient care, which usually operate in silos," says **Dr. Rani Srivastava**, CAMH chief of Nursing & Professional Practice. She notes that staff satisfaction with TDM is high, which is essential for implementation.

Both peer and staff relationships are key components of the transition. At CAMH, paid peer support workers lead a client drop-in group, maintain contact by phone or through casual meetings, and connect clients with local agencies, notes CAMH site lead **Elizabeth Budd**. Inpatient staff stay in touch until a therapeutic relationship in the community is established.

In the project's final phase, lead Dr. Cheryl Forchuk of London's Lawson Health Research Institute will work with CAMH and eight other sites on strategies to sustain TDM.

Dr. Fang

Senior Scientist



Nasal spray has potential to treat depression

A nasal delivery system that carries a protein peptide to the brain has potential to treat depression, according to research by **Dr. Fang Liu**. The peptide, which Dr. Liu had previously found was effective in reducing depression-like symptoms, needed a non-invasive delivery system to the brain. Her recent study, published in *Neuropsychopharmacology*, showed that nasal delivery reached the right part of the brain and relieved depression-like symptoms in preclinical models.

"This research brings us one step closer to clinical trials," says Dr. Liu. In ongoing lab research, her team is experimenting to see if they can make the peptide break down more slowly, and travel more quickly in the brain, to improve its antidepressant effects.

[Neuropsychopharmacology article](#)



Dr. Paul

Fletcher

Senior Scientist

In a new study funded by the Canadian Institutes of Health Research, Dr. Paul Fletcher and post-doctoral fellow Dr. Fiona Zeeb are examining the role of serotonin in addiction-related behaviours. Their research investigates the potential for drugs acting on a serotonin brain receptor to treat addiction, impulsiveness and over-eating.

Adulthood

Burden of mental illness and substance use disorders

Globally, mental illnesses and substance use disorders are the most disabling conditions for individuals.


The most recent Global Burden of Disease Study, published in the *Lancet*, showed that these conditions are the leading cause of years lived in poor health, more than eight other categories of disease. **Dr. Jürgen Rehm** was a co-author on this study.

Determining the relative impact of different illnesses and diseases on people's lives is important for health care planners and policy-makers, as it can help guide decisions on distributing health care resources.

Depressive disorders accounted for more years lived with disability than any other mental illness, at 41 per cent, followed by anxiety disorders, drug use disorders and schizophrenia. The study also examined premature death, using a measure called years of life lost. Among all mental illnesses and addictions, 81 per cent of early deaths were related to drug or alcohol use disorders.

These two figures—years lived with disability and years of life lost—are combined to determine a measure known as disability-adjusted life years. By this measure, mental illness and substance use disorders accounted for seven per cent of the total global disease burden, less than cancer or heart-related diseases, but more than HIV/AIDS and diabetes.

[!\[\]\(9c8ee003afcb6f6a71601185bbfeecdf_img.jpg\) The Lancet article](#)



Advancing recovery-oriented care through storytelling

Can clients' stories shift professionals' attitudes toward how they approach care? A study by **Dr. Sean Kidd** suggests they can. At CAMH, recovery-oriented care is a priority underlying service delivery. CAMH adopts a client-centred, collaborative approach, recognizing the importance of helping clients live purposeful lives. To advance this approach in inpatient mental health settings, Dr. Kidd studied the use of narrative, which has worked in other settings such as with stroke rehabilitation.

Over one year, 12 former inpatients spoke twice a month with staff on three hospital units, telling stories about their recovery, such as work or volunteering experiences. They also provided honest feedback on their care. Three other units served as a comparison group.

As reported in *Psychiatric Services*, the stories resulted in a shift in hospital staff's knowledge and attitudes toward a recovery-oriented framework. Staff described an improved sense of hope for clients and greater confidence of their impact, as well as more empathy and self-reflection. Speakers described feeling empowered and more confident. The Canadian Foundation for Healthcare Innovation funded the study.

 [Psychiatric Services article](#)

 [Recovery-oriented care video](#)



Reducing alcohol consumption cuts mortality

Alcohol use disorders are linked to a higher risk of disease, disability and death. By reducing drinking, the risk of death drops by more than a half, according to a new review by **Dr. Michael Roerecke**.

The review, published in the *Journal of Clinical Psychiatry*, pooled results from 16 studies that tracked adults after they were treated for alcohol misuse. Those who achieved abstinence had the greatest decline in risk of dying. But even those who curtailed drinking substantially decreased their risk.

The researchers concluded that any type of treatment—whether the goal is abstinence or reduced drinking—is better than none.

These results are encouraging, especially in light of the World Health Organization's 2014 *Global Status Report on Alcohol and Health*, which showed that more than 3.3 million deaths in 2012 were due to the harmful use of alcohol. Heavy alcohol use is also associated with mental illnesses, injuries, liver disease and certain cancers, as well as increased susceptibility to infectious diseases such as tuberculosis and pneumonia.

 [Journal of Clinical Psychiatry article](#)

Q & A

Meet Our Experts



Akwatu Khenti

CAMH's global mental health research has expanded significantly in the past three years under the leadership of Akwatu Khenti, director of the Office of Transformative Global Health (OTGH). When it was established in 2002, the office concentrated its efforts on international training programs and clinical capacity building. In 2012, the office joined CAMH's Social and Epidemiological Research (SER) department and quickly reoriented efforts toward collaborative and transformational research and research capacity building. Since then, Khenti and his team have successfully acquired research grants for projects in India, Peru, Haiti and Tanzania, as well as Canada.



Transformative Global Health video

Q. Of the many important projects underway, is there any one in particular that's worth noting?

A. Currently the biggest project is an initiative in Gujarat, India, in collaboration with the Indian Law Society and the World Health Organization (WHO). We have a Grand Challenges grant to study the effectiveness of WHO's *QualityRights Tool Kit* in improving mental health care in six hospitals serving 50,000 patients. The tool kit provides direction on improving facilities, providing human rights training, and introducing policies to support anti-stigmatizing treatments and client-centred recovery, as well as training for non-professionals to support clients and families. The potential impact is huge.

 [QualityRights Tool Kit](#)

Q. One key area you're researching is stigma.

A. We have a study on reducing stigma among health professionals in seven community health centres (CHCs) in Toronto that serve diverse and marginalized populations. It's a multi-faceted intervention, including training, leadership development, public education, a recovery-based arts component, and policy and procedure analysis. First we ran a three-year pilot project to develop this intervention, and preliminary results were positive. Earlier this year, we received a grant from the Canadian Institutes of Health Research to run a full trial of the intervention. It's a cluster randomized controlled trial (RCT), meaning some centres will get the anti-stigma intervention and others won't, so we can look at its impact.

Q. How does this relate to your international work?

A. We'll be studying this same anti-stigma intervention in Peru, with a Grand Challenges grant. But our research in this area began in 2006, after an external review of our work in South America showed that one of our most significant outcomes was a reduction in stigma. Health professionals who were previously hesitant or unwilling to treat clients with substance use or mental health problems reported a change in attitude and practice. CAMH's interprofessional and biopsychosocial approach to treatment provided an impetus, and enhanced our international learners' motivation to approach these clients in a different way. We realized that we could make both a global and a local impact in reducing stigma. This realization led us to redouble our efforts in this area.

Q. Your projects are diverse in scope and based in four continents. How did you get them off the ground?

A. I'd say that it's essential to have strong project teams, take time to build solid relationships, be opportunistic about funding opportunities, and be persistent. We've had many rejections and kept on applying. During the interim, we conducted many low-cost academic exchanges to maintain international relationships and to keep commitments strong. Our ability to have a global reach is only possible because all work is done through interdisciplinary teams, which is crucial for our partners because of resource limitations in low-income countries. Having flexibility allowed us to adapt to a steady stream of changes among the donor community.

Q. How do you ensure you are not imposing your approaches and values on other cultures?

A. We approach all our work as respectful learners, expecting that some technologies will be culturally and socio-economically relevant while some will not. We plan a process of cultural screening as a first step in our collaborations. CAMH also has an incredible array of multicultural expertise and talent that allows us to work well within many different cultural settings. For instance, we've developed culturally adapted cognitive-behavioural therapy (CBT) resources in French, Spanish and English, which are being used in related efforts abroad. We're planning a pilot study in Haiti, where spiritual leaders will be taught this culturally-adapted CBT. Our co-investigators are the heads of Haiti's main spiritual traditions and religions—voodoo, Catholic and Protestant. The nature of the work and teams give our collaborations a lot of credibility on the ground.

We also need to contribute as much as we can to alleviate the tremendous inequities in mental health care, which are an affront to human dignity. I've seen much unnecessary human suffering. This realization keeps me going when the going gets tough.

A close-up portrait of Dr. Shelley McMMain, a woman with short, dark brown hair, smiling warmly. She is wearing a light-colored, possibly white, button-down shirt. The background is a soft-focus outdoor setting with trees and foliage. On the left side of the image, there is a decorative graphic consisting of overlapping, semi-transparent geometric shapes in shades of light blue and white.

Dr. Shelley

McMMain

Scientist

While standard one-year dialectical behaviour therapy (DBT) is effective for people with borderline personality disorder who self-harm, most DBT programs have lengthy wait lists. In practice, DBT is often abbreviated, despite little evidence to justify this practice. Dr. Shelley McMMain and her team are determining the clinical and cost-effectiveness of a six-month versus standard course of DBT in a five-year study funded by the Canadian Institutes of Health Research.


Late Life



Alzheimer's changes may begin in childhood

People who carry a high-risk gene for Alzheimer's disease show brain changes beginning in childhood, decades before the illness appears. The gene, called SORL1, is one of a number of genes linked to a higher risk of late-onset Alzheimer's disease. In a study in *Molecular Psychiatry*, **Dr. Aristotle Voineskos** and colleagues showed that a specific version of SORL1 was linked to Alzheimer's-related brain changes in children as well as adults. Researchers used a type of brain imaging called diffusion tensor imaging (DTI) as well as post-mortem tissue, in both healthy people and those with Alzheimer's, to determine this link.

Alzheimer's disease results from a combination of factors in addition to a person's genetic profile—an unhealthy diet, lack of exercise, smoking and high blood pressure. "This gene has a relatively small effect, but the changes are reliable and may represent one 'hit' among a pathway of hits required to develop Alzheimer's disease later in life," says Dr. Voineskos.

 [Molecular Psychiatry article](#)



Preventing dementia

By the time someone is diagnosed with Alzheimer's disease, the person's brain is already damaged, so treatments don't work well. The idea of preventing illness before symptoms occur is the purpose of a major new CAMH study. Researchers will test the combination of a painless brain stimulation treatment and cognitive skill-building exercises with two groups of older adults at high risk of developing Alzheimer's—those with depression or with mild cognitive impairment.

"Our approach will stimulate neurons in the brain and strengthen cognitive skills, which we hope will prevent the brain damage associated with Alzheimer's, and prevent or delay the diagnosis," explains lead investigator **Dr. Benoit Mulsant**. The study, called PACT-MD, (Preventing Alzheimer's dementia with Cognitive remediation plus tDCS in MCI and Depression) is supported by Brain Canada and the Chagnon Family.



Treating Alzheimer's agitation

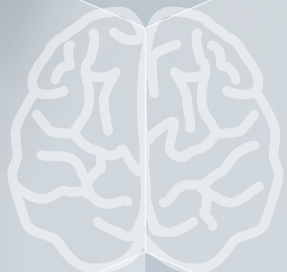
The agitated behaviour that occurs with Alzheimer's disease can be relieved by the antidepressant citalopram, according to a study published in the *Journal of the American Medical Association*, involving eight leading research centres in North America.

Dr. Bruce Pollock, who headed research at the CAMH site, found that citalopram significantly relieved agitation in patients with Alzheimer's disease, without the risks of serious side-effects associated with the use of antipsychotic medications. Symptoms of agitation—such as emotional distress, restlessness, aggression and irritability—are a major reason why people go into long-term care prematurely.

 [Journal of the American Medical Association article](#)

Q & A

Meet Our Experts



Etienne Sibille

Dr. Etienne Sibille is the new Campbell Family Chair in Clinical Neuroscience in the Campbell Family Mental Health Research Institute at CAMH. Recruited from the University of Pittsburgh, Dr. Sibille's expertise is in the molecular biology of depression and aging, with a strong translational emphasis. He is also a professor in the Department of Psychiatry and the Department of Pharmacology and Toxicology at the University of Toronto.

Q. Why study both depression and aging?

A. Depression has a negative effect on brain functioning. And the risk of depression and other brain-related illnesses such as Alzheimer's disease increase as we age. Indeed, it's been proposed that depression is an illness of accelerated aging.

At the biological level, we've found a striking overlap between the molecular pathways associated with age-related changes over a lifetime, and depression and other psychiatric and neurodegenerative illnesses.

So I realized that studying the normal aging of the brain could help us understand the cellular and molecular mechanisms underlying changes in depression. My focus is to use this approach to identify new targets for treatment or prevention of depression.

Q. Can you describe some of your findings?

A. My lab has shown that aging has a large yet specific effect on multiple genes, influencing how these genes function and produce proteins. We've shown that many of these age-related changes are strikingly similar to those we see in brain-related illnesses, including depression.

One example is a protein called brain-derived neurotrophic factor (BDNF). BDNF is important for brain development and healthy functioning of neurons. We know that BDNF levels are lower in people with mood-related disorders, and in healthy older adults. We've now showed that BDNF levels decline over time in both cases, although it happens earlier in depression.

Another of many examples is with the genes coding for a type of chemical called an inhibitory neurotransmitter, which helps maintain chemical balance in the brain.

Q. If these biological changes are linked to depression, wouldn't all older adults experience depression?

A. It's true that biological changes alone do not necessarily lead to symptoms of depression among older adults.

To understand why, I have proposed a model of age-by-disease interaction. Aging is a continuous lifelong process, in which our bodies constantly adapt to counter biological changes related to aging, and to maintain a biological balance. Many of these changes are essential responses to the environment.

We believe that problems emerge when the timing of these changes is off. At a younger age, for example, lower BDNF levels might disrupt key neural networks and lead to problems with mood regulation. Most older adults would have adapted to the decline in BDNF levels over time, and don't show symptoms.

Q. So you would use the age-by-disease model to understand these differences?

A. Yes. First, we need to understand which biological and cellular processes in the brain are engaged during aging. Second, we look for changes in the same processes in depression. The key is then to identify which other factors—or moderators—affect the trajectory of those changes.

Moderating factors, which may be environmental or genetic variations, may accelerate or slow down changes in BDNF or chemical inhibition, especially in a middle-aged person. If we can identify the overlap between age, brain illnesses and moderating factors, it might provide a target for intervention.

We are also looking at targets that delay age-related changes, which could protect some people from developing depression.

Q. What other projects are you working on?

A. One project involves identifying genes related to chemical inhibition in depression. We are broadly looking at biological changes related to inhibition that involve GABA, which is the major inhibitory neurotransmitter.

We are also using genetic variations as a way to translate our basic science findings of the human brain to population studies. I've begun working with data from two large studies that track people as they age—the Health ABC and the Cardiovascular Health Studies. We are studying physical and mental changes related to genetic variations, among the genes identified in our studies of aging and depression.

Q. Interestingly, you apply a variety of approaches in your work.

A. My background is in molecular biology, working with animal models. Because of the limitations of these models, I thought it was important to study actual occurrences of depression from the genes and brain tissues of people affected by this illness. Using Columbia University's and then the University of Pittsburgh's post-mortem brain banks, I was able to identify a new cellular target related to GABA, the major inhibitory chemical, and somatostatin, a cellular marker of specific GABA neurons. Based on these findings, I was then able to develop more informed animal models. I continue to use both post-mortem tissue and animal models in my work, combined with molecular and bioinformatics approaches.

CAMH Research & Highlights Awards

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2014 U.S. Brain & Behavior Research Foundation
NARSAD Young Investigator Grants
Dr. Faranak Farzan, Dr. Colin Hawco, Dr. Sanjeev
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2014 Vanier Canada Graduate Scholarship
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Canadian Institutes of Health Research



Dr. James Kennedy

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Brain & Behavior Research Foundation



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NARSAD Independent Investigator
Brain & Behavior Research Foundation



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Highly cited researcher, 2002–2012
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2013–2014

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