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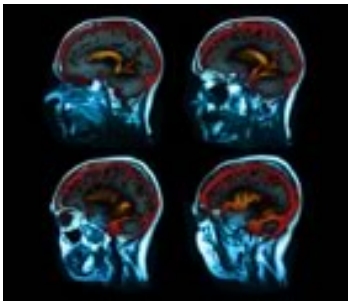
CAMH Science: Centred on Discovery

Science Synopsis from the Research Program
Volume One, Issue Two



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From the Desk of Darryl Yates, Director of Research Operations

Over the last few months, we worked hard to update the Research Functional Plan. This is the document that guides the Research Program's role in the Queen Street site redevelopment. And am I pleased to say that we proposed a Plan that strategically fosters research at CAMH over the coming years.

I am inspired by our renewed vision for Research – a vision that focuses on integration. Our extensive planning process enables the Research Program to integrate smoothly with CAMH's new vision for mental health and substance use. As the Queen Street site is transformed, we will be creating facilities that support clients' dignity, recovery and transition back into the community, while integrating the best in research, clinical care, teaching, health promotion and policy at one site.

We are committed to working together so that our scientists conduct collaborative research

across disciplines and change how people receive care. This exciting environment increases our opportunities to work together to generate timely and relevant research. We will also be in a better position to translate these scientific discoveries into improved clinical care, prevention and intervention initiatives, and public policy. Visit Redeveloping the Queen Street site for more information on what's in store for the renewed CAMH.

Thank you to all of you who contributed to the updated Functional Plan. I would especially like to thank Debbie Thompson, Manager of Research Operations, for her tireless efforts in assisting me to ensure this project stayed on track. It was an exhaustive task, but one that will bring immense benefits to the Research Program, to CAMH, and to the community.

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Talk Back

Got a story idea you'd like to share? Contact the editor at leah_kirkpatrick@camh.net. All suggestions and comments are welcome.

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Ontario Tobacco Research Unit Develops New Online Tobacco Control Course

Under the strategic direction of Joanna Cohen and Roberta Ferrence the Ontario Tobacco Research Unit (OTRU) developed a free online tobacco control course entitled *Tobacco and Public Health: From Theory to Practice.* more

CAMH Welcome's New Scientist

We are pleased to welcome Bernard Le Foll, MD PhD to CAMH. Coming to us from the National Institutes of Health in the United States, Dr. Le Foll is the Head of Translational Addiction Research Laboratory. We are looking forward to exciting and meaningful research coming out of this newly established nicotine research lab. In this role Dr. Le Foll will examine animal models of nicotine addiction and he hopes to pursue both clinical and PET research. In addition to his research activities, Dr. Le Foll will be seeing patients when this is arranged.

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Mental Health Spotlight

See Dr. Paula Goering's feature on mental health in a recent CHIR research spotlight. Visit IHSPR Research Spotlight - CIHR for more information.

2005/2006 Research Annual Report

Visit CAMH Research Annual Report to view highlights of our many accomplishments over the past year (PDF only).

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Profile: Louis Gliksman and the WHO

Brazil, Geneva, El Salvador, Montreal, Guatemala. You might be asking yourself what these locations have in common. The answer is Dr. Louis Gliksman. Still confused? As CAMH's Coordinator for the World Health Organization (WHO), Louis fosters connections that help build research capacity and generate policies and strategies to improve health conditions in developing countries.

According to Louis, CAMH's relationship with the WHO dates back to the former Addiction Research Foundation. "Originally CAMH was a WHO *Centre of Excellence.* Now as a WHO/Pan American Health Organization (PAHO) Collaborating centre we work with both the regional office (PAHO) and the central office in Geneva on a variety of projects. We are one of a handful of collaborating centres focused on mental health and addictions, and this gives CAMH an opportunity to participate in very meaningful and innovative projects."

For example, CAMH worked with the WHO to develop some significant products, including a report on the Global Burden of Disease and a book entitled Neuroscience of Psychoactive Substance Use and Dependence. Also, the Mental Health Global Action Programme (mhGAP) trains and educates researchers from

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developing countries. For 4 to 5 months, a student works with a CAMH mentor to develop a project that he/she implements in his/her home country. The CAMH mentor continues to act as an advisor to the project, once a student returns home. As examples, we had a student from Brazil, who developed a project designed to address barriers in healthcare for people living with HIV. CAMH staff are also working with another student from Tanzania, who is developing a project for dealing with the heroin problem.

"The Global Alcohol Database (GAD) is another really exciting WHO initiative," says Louis. As the Principal Investigator, it is Louis's responsibility to ensure the database is regularly updated with new data on consumption, trends, morbidity and mortality rates from around the world. Louis also ensures that the database is accessible from across the world. This requires ongoing monitoring of the literature, accessing new databases and ensuring that the technology is user friendly.

The database is an extremely important and useful tool, as it gives researchers a picture of what the important issues are in any given country. It also helps inform decisions on what research should be looking at, and guides policy reform and development on a global scale.

Currently, Louis is working on a project that is building research capacity in 3 Latin American countries. Working with Dr. Gaston Harnois, from the collaborating centre at McGill University this project will train people on how to conduct research and implement health improvement strategies based on their findings.

"We're working with motivated individuals from Guatemala,

Nicaragua and El Salvador, who don't have experience obtaining the necessary data to effect real change," says Louis. "Together with my colleagues at McGill, PAHO, and our partners in these countries, we are working to conduct research that will help them develop policies and programs to address important health issues."

By working together through CAMH's designation as a WHO/ PAHO Collaborating Centre, developing countries gain expertises, policies, programs and a network of colleagues that they never had before. It is an opportunity for our researchers and other staff to expand their networks and increase their understanding of mental health and addiction issues around the world.

For Louis, the most meaningful aspect of these extensive collaborations is that, "we gain just as much, or more, than we give. We live in a diverse, multi-cultural society. Working with colleagues in places like Brazil and El Salvador, we learn invaluable information on cultural aspects of collecting data, how to over come cultural barriers, and develop useful networks around the world that continue to enhance Research at CAMH long after the project is finished."

Visit WHO/PAHO Collaborating Centres for more information.

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Study Identifies Vulnerability to Depression Relapse

A recent CAMH study showed that individuals who recover from depression may continue to be at risk for relapse, if brief feelings of sadness trigger depressive thinking styles. This is the first study to make the link between these differences in thinking styles and the prediction of illness relapse, following successful treatment for depression. The study results suggest that treatment approaches directly targeting thinking styles may be an effective tool in preventing depression relapse.

Lead by CAMH scientist Dr. Zindel Segal, the new study revealed that individuals who achieved clinical remission from depression through antidepressant medication showed greater levels of depressive thinking after a procedure that caused temporary sadness, compared to those who had received cognitive behaviour therapy. Regardless of the type of treatment, the magnitude of depressive thinking revealed while patients were briefly sad was a significant predictor of relapse.

The data showed that 51% of participants had a relapse of depression during the follow up phase of the study. Classifying patients on the basis of the how significant a change in depressive thinking they showed, following an

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experimental induction of sadness, allowed for 81% of relapsers to be correctly identified. These results demonstrate a residual but increased risk for relapse that has not been fully addressed by treatment.

Major depression is now the leading cause of disability globally, and more than 50% of people diagnosed with clinical depression will experience a relapse in symptoms. Yet, routine clinical management of depression targets reducing symptoms during the acute phase of the illness. Little attention is paid to strategies for reducing the risk of relapse, or to measures that are able to identify those people in remission who are at risk for a relapse of depression.

This work holds promise for the design of more effective treatments that, in addressing this vulnerability, will allow people to get well and stay well longer. Dr. Segal is already studying the effects of a novel treatment that teaches patients how to address these mood-linked changes in thinking styles through the practice of mindfulness meditation.

Visit http://archpsyc.ama-assn.org for a full copy of Dr. Segal's paper entitled "Cognitive Reactivity to Sad Mood Provocation and the Prediction of Depressive Relapse."

Click here to view CAMH's press release on this study.

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High Rates of Multimorbidity Revealed

There is a large body of research available about the prevalence and impact of people who experience both a mental disorder and substance use disorder, a condition referred to as co-morbidity or concurrent disorder. However, there is little discussion of the prevalence and impact of multiple mental disorders combined with multiple substance use disorders, multi-morbidity.

In a recent paper, CAMH scientists sought to fill this information gap. They conducted a study that looked at the rates of clusters of psychiatric symptoms among clients with a substance use disorder.

All study participants were attending an outpatient addiction treatment program. Using a standardized test, each study participant was screened for the presence of specific psychiatric symptoms. These symptoms were grouped in clusters such as depression, anxiety or conduct disorder.

The data showed that approximately 70% of all clients screened positive for at least one cluster of psychiatric symptoms. Of this group, 27% screened positive for one, 19% screened positive for two, and 22% screened positive for three or more clusters.

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Also, those clients with more substance use disorders presented with more psychiatric symptom clusters. Among clients with symptoms of a least one cluster of psychiatric symptoms, approximately 28% presented with two, and 12% presented with three problem substances.

Results also showed that multi-morbidity was significantly associated with female gender, unemployment, lower social support, cannabis-related problems, fewer legal problems and increased treatment engagement.

Current treatment approaches for co-morbidity do not appropriately address the complexity of multiple disorders and associated problems. The results of this study point to the need for policy makers, program administrators and clinicians to plan appropriate and more integrated approaches to substance abuse and mental health treatment and support.

Click Overlap of Clusters of Psychiatric Symptoms Among Clients of a Comprehensive Addiction Treatment Service to view a copy of this paper.

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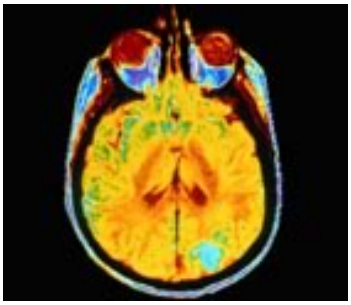
The Next Therapeutic Frontier for Schizophrenia Treatment



The Stanley Medical Research Institute (SMRI) recently awarded Dr. David Mamo and Dr. Shitij Kapur a CAN$330,000 grant to study l-stepholidine, a compound derived from of a naturally occurring Chinese herb called *Stephania intermedia*. The aim of this positron emission tomography (PET) study is to confirm binding of l-stepholidine to dopamine D2 receptors in healthy human subjects; obtain supporting evidence of its safety and tolerability; and predict effective dosages for future clinical trials in people with schizophrenia.

PET imaging has already contributed to our understanding of how anti-psychotics work and led to a better understanding of effective dose range in clinical practice. More recently this group has used PET imaging in early drug development to predict clinically effective dosing strategies in clinical trials.

SMRI granted this award following a highly competitive grant application process, from which only 4 of 55 treatment trial applications were successful. In this new study, Dr. Mamo and Dr. Kapur will build on previous SMRI-funded work that showed that l-stepholidine binds to both the D1 and D2 receptors in living rodents without causing neurological side

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effects. These findings are consistent with previous pre-clinical work from China, suggesting that l-stepholidine is both a D2 antagonist (like standard anti-psychotics) and also a D1 agonist (which has theoretical implications for addressing cognitive and negative symptoms). These factors make it a potentially new treatment for schizophrenia.

Anti-psychotic drugs are generally quite effective in managing delusions and hallucinations. However, they have limited impact on other core symptoms of schizophrenia including difficulties thinking, reasoning skills, and negative symptoms such as social withdrawal and lack of interest in activities. These cognitive and negative symptoms are closely associated with social and interpersonal functioning. Therefore, effectively addressing these symptoms is the next therapeutic frontier in the goal of improving recovery outcomes for an otherwise devastating illness.

All available anti-psychotic drugs are antagonists at the dopamine D2 receptors, and binding to D2 receptors predicts their clinical effects on delusions and hallucinations but not their effects on cognitive and negative side effects. One of the most promising targets to enhance these cognitive difficulties in schizophrenia is a treatment that binds to another subclass of dopamine receptors, the D1 receptor. Scientists are hopeful that their work will show that l-stepholidine will be the compound that fills this treatment gap.

When Dr. Mamo and Dr. Kapur successfully complete this study, this will mark the first time that CAMH scientists translated what they learned from their own pre-clinical animal findings to a clinical trial. Moreover, if their work does

support their hypothesis, we will have a model for a new treatment for schizophrenia that focuses on negative symptoms - a critical step that could revolutionize the management of schizophrenia.

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SAD and Obesity: What's The Link

In a recent study, CAMH researchers examined the link between season of birth and body weight in women with Seasonal Affective Disorder (SAD). Led by Dr. Robert Levitan and Dr. James Kennedy, the study examined whether the season a person was born in impacted body weight regulation in individuals with SAD. Their investigation included possible interaction effects with the 7R allele (specific section of DNA coding) of the dopamine-4 receptor gene (DRD4), the gene that influences weight gain by causing loss of sensitivity to the brain chemical dopamine.

The study revealed that those women born in the spring and carrying the 7R allele (designated the high-risk group) had an average maximum Body Mass Index (BMI) 26% higher than those individuals born in other seasons and without the 7R allele (designated the low-risk group).

These investigators also looked at lifetime rates of obesity and morbid obesity in both the high-risk and low-risk groups. The high-risk group was significantly more likely to experience obesity or morbid obesity. 53% of the high-risk group had obesity at some point in their lives, compared to 20% of the low-risk group. Looking at morbid obesity, 24% of the high-risk group experienced

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this condition compared to just 4% in the low-risk group.

At a genetic level, these results expand our understanding of weight gain and obesity in women with SAD by suggesting that factors linked to birth season, such as early exposure to hormones tied to seasonal light/dark cycles, interact with the DRD4 gene to influence body weight regulation in this population.

Overall, these results also point to a novel interaction between a person's genes and the environment during the early stages of brain development, which triggers weight gain and obesity later in life. The authors propose that this phenomenon is the result of a *seasonal thrifty phenotype,* a historical behavioural strategy programmed in our genes that enhanced survival in northern latitudes. Thousands of years ago, characteristics seen is SAD, such as increased eating and decreased activity, were adaptations to or predictors of seasonal famine in areas further from the equator. However, in today's environment of plentiful food, these characteristics create an increased risk for obesity in women with SAD.

Click A Birth-Season/DRD4 Gene Interaction Predicts Weight Gain and Obesity in Women with Seasonal Affective Disorder: A *Seasonal Thrifty Phenotype Hypothesis* for more information.

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