CAN-ACN
CANADIAN ASSOCIATION FOR NEUROSCIENCE
ASSOCIATION CANADIENNE DES NEUROSCIENCES

# 12th Annual
# Canadian Neuroscience Meeting

## Organised by the Canadian Association for Neuroscience

### Press releases and Information for the Media

Annual Meeting: **May 13 – 16, 2018**

Sheraton Wall Centre Vancouver

1088 Burrard Street, Vancouver, BC, V6Z 2R9

https://can-acn.org/meeting-2018

Public Lecture: **May 12th, 2018, 4PM – 6 PM**

Science World Vancouver

1455 Quebec St, Vancouver, BC V6A 3Z7

## Contents

## 12th Annual Canadian Neuroscience Meeting - General Information

This meeting is presented by the Canadian Association for Neuroscience - Association canadienne des neurosciences. Here you will find general information about our Association, which is an association of neuroscientists dedicated to the promotion of all fields of neuroscience research. Our press releases follow.

**CAN-ACN Mission**

The purpose of the Canadian Association for Neuroscience is:

1. To promote communication among neuroscientists throughout Canada.
2. To represent the interests of Canadian neuroscientists at national and international levels.
3. To promote research in all disciplines contributing to the understanding of the nervous system.
4. To contribute to the advancement of education in the Neurosciences.
5. To provide for and assist in the dissemination to the general public of the results of current Neuroscience research and its significance in relation to health and disease.
6. To raise funds and to provide income for the above purposes.

The Canadian Association for Neuroscience is a registered **not-for-profit association**.

**CAN-ACN Leadership - Executives**

- President: **Lynn Raymond**, PhD, University of British Columbia
- Vice-President (President-Elect): **Jaideep Bains**, PhD, University of Calgary
- Treasurer: **Derek Bowie**, PhD, McGill University
- Secretary: **Ed Ruthazer**, PhD, McGill University
- Chair of the Advocacy Committee: **Katalin Toth**, PhD, Université Laval
- Chair of the nominations committee: **Doug Munoz**, PhD, Queen's University

**2018 Meeting Organisation**

Chair of the 2018 Scientific Program Committee: **Shernaz Bamji**, PhD, University of British Columbia

Co-Chair of the 2018 Scientific Program Committee: **Paul Frankland**, PhD, University of Toronto

Chair of the Local Organizing Committee: **Timothy O'Connor**, University of British Columbia

**Members of the 2018 Scientific Program Committee**

- **Jean-Claude Béïque** – University of Ottawa
- **Maurice Chacron** – McGill University
- **James Fawcett** – Dalhousie University
- **Stephanie Fulton** – Université de Montréal
- **Michael Hendricks** – McGill University
- **Sarah McFarlane** – University of Calgary
- **Martin Paré** – Queen's University
- **Marco Prado** – Western University
- **Marie-Ève Tremblay** – Université Laval
- **Ian Winship** – University of Alberta

**CAN-ACN Administration**

Association Secretariat & Conference Management:
De Armond Management Ltd. secretariat@can-acn.org
**Pam Prewett, Jude Ross, Marischal De Armond**.

Chief Operating & Advocacy Officer:
**Julie Poupart**, PhD - info@can-acn.org

**Membership Information**

CAN-ACN membership is open to students, post-doctoral fellows and principal investigators actively engaged in neuroscience research in Canada and around the world.

**2018 Public Lectures**

Two public lectures will take place on May 12th 2018 at Science World. Open to all people interested in neuroscience. Admittance is free but limited.

**2018 Press releases**

You will find our press releases in the following pages. Our press releases are published on the EurekAlert! Website, the online, global news service operated by AAAS.

## Meeting announcement:
## 12th Annual Canadian Neuroscience Meeting, Vancouver, May 13 to 16, 2018

The Canadian Association for Neuroscience is pleased to announce it will hold its twelfth annual meeting in Vancouver, Canada, from May 13th to 16th, 2018. The meeting will gather neuroscientists from Canada and around the world to share their research on the brain and nervous system. All areas of neuroscience research will be presented.

"Our meeting is a great opportunity to see the breadth of neuroscience research that is done in Canada, and the advances we are making towards understanding the brain. These discoveries are the foundations upon which we will build to find therapies and treatments for the many illnesses that affect the brain", states **Lynn Raymond**, President of the Canadian Association for Neuroscience.

Two public lectures, on the timely topic of addiction, will be presented by two leading experts in the field: **Catharine Winstanley** and **Luke Clark**, both at the University of British Columbia. Dr. Catharine Winstanley's research has provided insight into the nature of addiction by developing a rat casino, which allows her to identify factors associated with gambling addiction in a controlled manner. Dr. Luke Clark will then present the latest research on gambling addiction in humans, and how the modern slot-machine is a form of gambling which is more harmful than others. Both lectures will be presented to the public at Science World in Vancouver.

The Canadian Association for Neuroscience is dedicated to promoting inclusivity, equity and diversity in neuroscience, and to this end, the meeting will feature an interactive luncheon workshop on this topic. Dr. **Judy Illes** will be leading the **Equity, Diversity and Inclusivity in Neuroscience workshop** (EDI-Neuro), which will serve to define the actions that our association can take to address these issues in coming years.

**Award presentations**

The Canadian Association for Neuroscience is proud to announce it will be awarding the 2018 **CAN Young Investigator Award** to **Karun Singh**, from McMaster University. Dr. Singh is a leader in stem cell research, human genetics and brain development.



Media contact: **Julie Poupart**, info@can-acn.org, 514-912-2405

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Dr. Karun Singh's research has made significant impact on our knowledge of signaling mechanisms that regulate brain development, and of the genetic risk factors underlying neurodevelopmental disorders. His work combines powerful human genetic studies and animal models. Using this approach, he has uncovered new disease mechanisms for autism spectrum disorder and schizophrenia, which are paving the way forward to identify new therapeutics.

https://can-acn.org/karun-singh-is-the-2018-can-young-investigator-awardee

The **CAN Outreach and Advocacy award** celebrates the efforts of groups working to increase awareness of neuroscience research and to ensure that a connection between the lab and the public is maintained. This year's winners are an impressive **group of graduate students from the University of British Columbia** who have developed an original and interactive way of presenting neuroscience research to the public: an online collection of cartoons titled "**Neuroscience through the ages**", which are collected on this website:

https://www.historyofneuroscience.com/

View the prize announcement here:

https://can-acn.org/neuroscience-through-the-ages-wins-2018-can-advocacy-award

The full program of the meeting is available online at:

https://can-acn.org/2018-meeting-program

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About the Canadian Association for Neuroscience:

The Canadian Association for Neuroscience is the largest association dedicated to the promotion of all fields of neuroscience research in Canada. The association has been organizing a yearly annual meeting since 2007. Learn more about our meeting at:

https://can-acn.org/meeting-2018

Please contact **Julie Poupart**, Chief Operating & Advocacy Officer for the Canadian Association for Neuroscience, for further information, to receive a press pack, or to request an interview with a neuroscientist. info@can-acn.org.

Event summary text:

The 12th annual Canadian Neuroscience Meeting will bring together over 700 neuroscientists from Canada and abroad to share the latest discoveries about the brain and nervous system. This meeting is an opportunity to learn more about all areas of neuroscience research, and meet neuroscientists. Among the highlights of the 2018 meeting are public lectures on the topic of addiction, a workshop on the important topic of Equity, Diversity and Inclusivity in Neuroscience and award presentations.

## Information about: 2018 CAN-ACN Public lecture May 12th, 4 – 6 PM

The Canadian Association for Neuroscience is proud to announce the 2018 Public lectures will feature two leading Canadian experts on the topic of addiction.

**Date**: Saturday, May 12th, 2018 – 4-6PM

**Location**: Telus Science World, 1455 Quebec St, Vancouver, BC V6A 3Z7 View on Google maps

**Tickets**: Get your free tickets on EventBrite

**Host**: Dr. **Liisa Galea**, Director of the Graduate Program in Neuroscience at UBC

**Speakers**:

**Dr Catharine Winstanley, PhD**
Associate Professor, Department of Psychology, University of British Columbia

### Against the odds: insights into the nature of addiction from studying decision making in rats

If we knew why some individuals are catastrophically affected by addictions, whereas others are simply able to enjoy addictive drugs recreationally, we would be able to design effective treatments to help vulnerable individuals. Whether someone is dependent on a chemical substance like cocaine, or has developed a behavioural addiction such as gambling disorder, the maladaptive choice to pursue the addiction at the expense of other goals lies at the heart of the problem. Indeed, individuals with an addiction disorder, or who later develop problems with addiction, score poorly on laboratory-based decision-making tests that involve the weighing of costs and benefits. One hypothesis is that decision-making impairments may be compounded as the addiction develops because of the way in which addictive drugs, and also engagement in addictive behaviours, affect brain function, biasing the decision-making process in favour of the addiction. Choosing to abstain from the addictive substance or behaviour then becomes increasingly difficult. We have successfully developed an animal model of this kind of cost/benefit decision making: the rat Gambling Task (rGT). On both human and animal tests, subjects choose between four different options, each of which is associated with different amounts of potential reward and loss. By avoiding high-risk, high-reward options, subjects can maximise gains.

Most rats develop this optimal strategy, although some animals instead favour the risky options. These risk-preferring rats are uniquely and adversely affected by taking cocaine: their decision making gets worse and they show increased drug-seeking in withdrawal indicative of greater relapse risk. Making risky choices therefore appears to be associated with greater sensitivity to the negative effects of an addictive drug. Furthermore, adding the kind of sensory feedback common to modern slot machines increases risky choice.

**Dr Luke Clark**
Director, Centre for Gambling Research at UBC
Department of Psychology

### Deconstructing the modern slot machine: gambling, game features and addiction

Gambling is a widespread form of entertainment in Canada and across much of the world, with 73% of the BC population reporting gambling in the past year. For some people, gambling behaviour becomes excessive, and Gambling Disorder is a recognized mental illness that is now classified alongside the substance addictions in psychiatry, as the prototype 'behavioural addiction'. Surprisingly, there is not yet a strong scientific foundation for how gambling (and other behaviours such as video gaming) can become 'addictive' in ways that are comparable to drugs of abuse. This talk will focus on research from psychology and neuroscience, considering how problem gambling develops. Part of the answer lies in personal vulnerability factors that cut across addictive disorders, including impulsivity as a personality trait and changes in the brain dopamine system. But personal vulnerabilities are not the full story: gambling products also play a role in the development of gambling problems, such that some forms of gambling are more harmful than others. Much of our research focuses on modern slot machines as a more harmful form of gambling. These games contain an array of psychological ingredients including near-misses and sensory feedback, which appear to amplify reward-related brain activity, especially in vulnerable individuals. Together, these features create a state of immersion that is also predictive of gambling problems.

More information: https://can-acn.org/can-2018-public-lectures

## Karun Singh is the 2018 CAN Young Investigator awardee

The Canadian Association for Neuroscience (CAN) is proud to announce that Karun K Singh, from McMaster University, will receive the 2018 CAN Young Investigator Award at the upcoming 12th Annual Canadian Neuroscience Meeting in Vancouver, on May 15th, 2018.

**Karun Singh: A leader in stem cell research, human genetics and brain development**

"*The quality of Dr. Singh's research is excellent, providing novel insights to molecular mechanisms of neuronal development with important implications for human health. The quality of his research arises from the application of a combination of cutting edge technologies and rigorous, thorough experiments proving each scientific finding. Dr. Singh has a dedication to link fundamental findings to disease processes*" says Kurt Haas, Ph.D., Full Professor at the University of British Columbia and Researcher at the Djavad Mowafaghian Centre for Brain Health.

Dr. Karun Singh's research has made significant impact on our knowledge of signaling mechanisms that regulate brain development, and of the genetic risk factors underlying neurodevelopmental disorders. Neurological disorders of the developing brain such as autism impacts 1 in 66 individuals in Canada while schizophrenia affects 1% of the population. Affected individuals and families are burdened by life-long health, social and economic issues. Unfortunately, there are no specific therapies for individuals because these disorders remain poorly understood. However, since neurodevelopmental disorders have a strong genetic basis, this provides a starting point to identify underlying disease pathogenesis mechanisms.

Dr. Singh's work combines powerful human genetic studies and animal models. Using this approach, he has made novel insights into how autism and schizophrenia risk genes disrupt neural development. For example, in complex brain disorders where there is a loss of multiple genes (named microdeletions), Dr. Singh's team recently identified that in each disorder, a single gene plays a strong role in the development of the disease. In addition, his work has uncovered that patient-derived mutations in multiple genes disrupt synaptic communication between neurons in the brain. These discoveries have pinpointed precise signaling pathways that are disrupted by mutations in high risk genes, providing a path forward for screening and identifying therapeutics that will reverse the neural impairments.

Building on these discoveries, Dr. Singh has established clinical and genetic sequencing collaborators to create a resource of human induced pluripotent stem cell (iPS cell) models to study brain development disorders. He is combining this approach with CRISPR gene editing to better dissect the precise mechanisms by which genetic mutations cause defects in neural development. His platform has established a mechanism to identify drugs that will be streamlined for future clinical trials.

In earlier work, Dr. Singh identified new signaling mechanisms regulating how the peripheral nervous system is established. These fundamental studies have uncovered how peripheral nerve cells form appropriate connections with target organs, while incorrect connections are eliminated. These studies provide new insights into pathology and treatment peripheral nerve diseases and injury.

His work has been published in several top neuroscience and genetics journals (both first and/or corresponding author) including Neuron, Nature Neuroscience, Molecular Psychiatry, American Journal of Human Genetics, and Cell Reports. In addition, his recent published papers have received a significant amount of attention in several media outlets. He currently holds a prestigious David Braley Chair in Human Stem Cell Research, and his success has allowed him to become the Neural Program Lead at the Stem Cell and Cancer Research Institute at McMaster University. His program is funded by multiple National and International sources including CIHR, NSERC, Ontario Brain Institute, Brain Canada, and the European Research Area Networks.

Dr. Singh has quickly become a leader in the brain development and neurodevelopmental disorders fields. His work is uncovering new disease mechanisms for autism spectrum disorder and schizophrenia, which is paving the way forward to identify new therapeutics. The Canadian Association for Neuroscience is very proud to present Karun Singh with the 2018 Young Investigator Award.

Learn more about Karun Singh
https://sccri.mcmaster.ca/people/karun-singh
https://fhs.mcmaster.ca/biochem/KarunSingh.html

Summary (75 words)

The Canadian Association for Neuroscience is proud to announce that **Karun Singh** (McMaster University) will receive the 2018 **CAN Young Investigator Award** on May 15th, 2018 in Vancouver. Dr. Singh's research has broadened our understanding of the genetics of brain development, and risk factors underlying neurodevelopmental disorders. His work has uncovered new disease mechanisms for autism spectrum disorder and schizophrenia which are paving the way forward to identify new therapeutics.



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## UBC Graduate Neuroscience team wins 2018 CAN Neuroscience Outreach & Advocacy Award

The Canadian Association for Neuroscience is proud to announce that a team from the Neuroscience Graduate Student Association at the University of British Columbia (UBC) who developed the "Neuroscience Through the Ages" project will be awarded a Neuroscience Outreach & Advocacy Award on Monday, May 14th 2018, during the 12th Annual Canadian Neuroscience Meeting.

Neurohistory Cartoons:

For the past year, the Neuroscience Graduate Student Association at UBC in Vancouver has been working on a project titled "Neuroscience Through the Ages" online interactive timeline. This project aims to present the history and fundamentals of neuroscience in an interesting and accessible manner – through the wonderful world of cartoon imagery. Over the past year, we have hired and collaborated with science cartoonists, Armin Mortazavi and Aarthi Gobinath, as well as website designer, Luis Bolanos. Content development begins with graduate students working individually or in groups to summarize the key findings and methodological advancements of specific historical researchers across many decades. These students gather information and pictures to help formulate a cartoon mock up (with suggested figures and captions). This information is provided to the cartoonist and the final products are made publicly available through an online interactive timeline. The timeline is a work in progress and can be found at www.historyofneuroscience.com or on twitter @neurohistoons.

The Canadian Association for Neuroscience is proud to support the development of this project, and applauds the originality, dedication and organisation of the NeuroHistory cartoons team.

Please visit the award webpage to learn more about the team of winners, and the project

https://can-acn.org/neuroscience-through-the-ages-wins-2018-can-advocacy-award

## 2018 Press releases

Press release about a presentation at the Canadian Association for Neuroscience meeting by Catharine Winstanley.

Press release embargoed until May 14th, 2018, 10:15 AM Pacific Time, 1:15 PM Eastern time

Title:

### Discovery of differences in the brains of rats classified as workers vs. slackers

Subtitle:

Catharine Winstanley at the University of British Columbia presents discoveries revealing the brain mechanisms involved in decision-making

Text:

A team of researchers led by Dr. **Catharine Winstanley** at the **University of British Columbia** have uncovered a network of regions in the brain that are involved in determining the choice of working harder to get a bigger reward or putting in a lesser effort and receiving a smaller reward. Understanding how the brain makes such decisions is one of the most fundamental questions in neuroscience and psychology, and sophisticated animal behavioural testing, coupled with advance brain imaging and stimulation techniques are shedding light on this important process. These results were presented at the 2018 Canadian Neuroscience Meeting, in Vancouver, May 14th, 2018.

Dr. Winstanley and her team have gained insight into decision-making by studying rats' performance of the "rat cognitive effort task" in which rats learn to earn sugary pellet treats by poking their nose into one of five response holes when a light inside one of the holes is illuminated. Before each test, the rats can choose to press one of two levers, one lever leading to an "easy" test, where the light is on for 1 second, with a reward of one pellet, and the second lever leading to a more attentionally demanding task, where the light is on for only 0.2 seconds, but results in a reward of two pellets. Researchers have found that some rats preferentially choose the easy test ("slackers"), while others prefer the more

challenging test ("workers"), and that this choice is not correlated with the rat's ability or efficiency at completing the task.

Through selective inactivation, the team has shown that many brain regions are involved in evaluating the required effort, and that different mechanisms are involved in accomplishing the task. Their experiments have also showed that there is not a simple decision-making center in the brain, but rather that signals through many brain regions and systems, which integrate information to measure information about risk, reward and effort required, resulting in the making of a decision.

"Our research shows that decision-making relies on brain regions involved in emotional responses (the basolateral amygdala) and translating those emotions into actions (striatal and dopamine systems) but also regions of frontal cortex (the anterior cingulate and medial prefrontal cortices) which are involved in detecting causal relationships between events and evaluating outcomes." says Catharine Winstanley.

Many psychiatric disorders are associated with defects in decision making, such as bipolar mania, psychopathy, drug and gambling addiction, and suicidal ideation. Understanding the mechanisms underlying the decision-making process could therefore lead to the identification of new targets of intervention in these disorders.

In healthy humans, the ability to choose an option that may be more difficult but may lead to a higher reward in the long run can have important consequence for individuals in terms of personal and economic success.

"The degree to which we are willing to select options that require more cognitive effort but which have the potential to lead to greater rewards has far-reaching consequences for our economic and personal success. The availability of a large range of behavioral tests in animals can help decipher the key players in the brain, in terms of brain regions and chemical signals, that are involved in making these decisions. Understanding how the brain makes decisions is one of the most fundamental questions in neuroscience today." says Catharine Winstanley.

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Funding source: Natural Sciences and Engineering Research Council of Canada (NSERC)



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Abstract:

**Deciphering decision making: exploring the neural systems underlying the evaluation versus employment of cognitive effort in rats**

*Catharine Winstanley, University of British Columbia*

The degree to which we are willing to select options that require more cognitive effort but which have the potential to lead to greater rewards has far-reaching consequences for our economic and personal success. However, relatively little is known regarding the neurobiology governing the adjudication and application of cognitive effort in the decision-making process. We therefore developed a decision-making paradigm for rats which requires animals to choose between two options that differ in the degree of cognitive effort required to attain success. In this rat cognitive effort task (rCET), animals decide at the start of each trial whether to perform an easy or difficult attentional challenge. In the easy condition, rats must correctly localize a visuospatial target which is illuminated for 1.0s, whereas on hard trials, the target is only presented for 0.2s. Hard trials are therefore more attentionally demanding, but accurate performance is rewarded with double the number of sugar pellets. We have observed that rats differ dramatically in their preference for the hard option, independent of their attentional ability, leading to their classification as either "workers" or "slackers". Through a series of pharmacological inactivation experiments, we have begun to characterize a network of regions within the affective corticostriatal loop that are involved in determining choice. Collectively, these studies indicate that the evaluation versus employment of cognitive effort are regulated by somewhat unique and dissociable neurobiological mechanisms.

Release Summary Text:
(75 words maximum)

Dr. **Catharine Winstanley** at the **University of British Columbia** have uncovered a network of regions in the brain that are involved in determining the choice of being a "hard-worker" or a "slacker". Understanding how the brain makes such decisions is one of the most fundamental questions in neuroscience and psychology, and sophisticated animal behavioural testing, coupled with advance brain imaging and stimulation techniques are shedding light on this important process.

Press release about a presentation at the Canadian Association for Neuroscience meeting by Naguib Mechawar

Embargoed until May 14th, 2018, 3:15 PM Pacific Time, 6:15 PM Eastern Time

Title:

## Child abuse has lasting effects in brain region regulating mood and emotions

Subtitle:

*Cellular and molecular modifications in the brain of child abuse victims could explain their increased vulnerability to stress-related psychiatric disorders, including depression and suicide.*

Text:

Psychiatrists have long known that child abuse increases a person's lifetime risk of psychiatric illness, including depression and suicide. New research by Naguib Mechawar and Gustavo Turecki from the McGill Group for Suicide Studies offers some explanation of the process through which abuse lastingly modifies brain wiring. Their research, which compare the brains of depressed suicides with or without a history of severe child abuse, and of healthy controls, identified important modifications in the Anterior Cingulate Cortex (ACC), a brain region critical for the regulation of moods and emotions. These findings were presented at the 2018 Canadian Neuroscience Meeting, in Vancouver, May 14th, 2018.

"Our results demonstrate that gene expression is strongly altered in a class of cells called oligodendrocytes in the ACC. This class of cells is responsible for producing myelin, which is an insulating compound that can be likened to the coating on electrical wires. Myelin-coated axons transmit nerve impulses efficiently, while a loss of myelin is generally associated with loss of transmission efficiency" explains Dr. Mechawar.

Using state-of the-art microscopy techniques, the researchers were able to measure the thickness of the myelin layer on individual neurons and found that this layer was specifically thinner in brain samples from individuals having suffered from child abuse.

"Our data clearly shows how severe child abuse modifies the architecture of the ACC by affecting the formation of the myelin sheath around neurons. This modification in a region



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that is key for mood regulation may underlie the increased vulnerability of abused individuals to mood disorders, such as depression“, concludes Dr. Mechawar.

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Funding source: ERAnet-Neuron, American Foundation for Suicide Prevention, Canadian Institutes of Health Research

Presentation abstract:

Naguib Mechawar | Douglas Institute (McGill University)

The impact of child abuse on oligodendrocytes and myelination in the human brain

Child abuse has devastating and long-lasting consequences on individuals, considerably increasing the lifetime risk of negative mental health outcomes. Yet, the neurobiological processes underlying this increase in vulnerability remain poorly understood. Using well-characterized post-mortem brain samples from psychiatrically healthy controls and depressed individuals who died by suicide with or without a history of severe child abuse, we investigated the hypothesis that, in the anterior cingulate cortex, epigenetic, transcriptomic and cellular adaptations associate with a history of child abuse. Our results showed cell-type specific changes in DNA methylation of oligodendrocyte genes and a global impairment of the myelin-related transcriptional program that specifically occurred as a function of child abuse, as these changes were absent in depressed suicides with no history of early life adversity. Furthermore, a significant reduction in the thickness of myelin sheaths around small-diameter axons was also found to associate with child abuse. These results indicate that child abuse may lastingly disrupt cortical myelination, a fundamental feature of cerebral connectivity.

Release Summary Text:
New research from the McGill Group for Suicide Studies shows that severe child abuse lastingly modifies brain wiring. The study compared the brains of depressed suicides with or without a history of abuse, and of healthy controls, identifying important modifications in the Anterior Cingulate Cortex (ACC), a brain region critical for the regulation of moods and emotions. This modification may underlie the increased vulnerability of abused individuals to mood disorders, such as depression.

Press release about a presentation at the Canadian Association for Neuroscience meeting by Stephanie Borgland

Embargoed until May 15th, 2018, 10:15 AM Pacific Time, 1:15PM Eastern Time

Title:

## An energy dense diet changes the brain and increases urge to eat

Subtitle:

Rats eating a "cafeteria-diet" show changes in the brain regions that integrate information about food and determines eating behaviour.

Text:

Research by Stephanie Borgland at the University of Calgary shows that giving rats unrestricted access to unhealthy foods for extended periods not only leads to obesity, but also to brain changes that makes food more attractive to them, even when their hunger should be satisfied. Specifically, Dr. Borgland's research identified modifications in endocannabinoid signalling in a brain region called the orbitofrontal cortex (OFC) of these obese rats. These unpublished results were presented at the 2018 Canadian Neuroscience Meeting, in Vancouver, May 15th, 2018.

The "cafeteria diet" is a model for feeding in which rats have, in addition to their regular balanced diet (or "rat chow"), access to an unlimited amount of high-fat, high-sugar foods, including chocolate and other treats. In Dr. Borgland's study, rats became obese after 40 days of 24h/day access to cafeteria diet, while rats with limited access (1h per day) did not. Previous work done in Dr. Borgland's laboratory had shown modification in signaling in a brain region called the Orbitofrontal Cortex (OFC) in obese rats, and this study aimed to better understand these modifications.

The OFC is a brain region located at the surface of the brain, above the orbits of the eyes. This brain region is involved in decision-making and receives information about food from the senses (taste, touch and smell) to register the value of food, and updates feeding behaviour based on this information. In non-obese animals, satiety following eating leads to food devaluation, and a reduced motivation to eat.

In obese animals however, previous work in the Borgland lab had shown a reduction in the inhibitory (or "stop") signals on a class of neurons called pyramidal neurons in the OFC. This study identified endocannabinoid signaling as a key player in this modification.

"Obesity is typically associated with an elevated level of endocannabinoids in both humans and rodents, so these results are not surprising. However, endocannabinoid signaling is much more complex than previously thought. Our research shows that endocannabinoid signaling selectively affect inhibitory signals onto the pyramidal neurons of the OFC. This effect is mediated through changes in specific receptors on the neurons but may also involve other types of cells in the brain, called astrocytes." Says Stephanie Borgland.

The world health organization indicates that obesity has nearly tripled since 1975 and estimates that 13% of adults in the world were obese in 2016. Obesity is a major risk factor for cardiovascular disease, such as heart disease and stroke, disorders such as osteoarthritis and some cancers.

"Future studies will need to further investigate the mechanisms through which endocannabinoids affect the motivation to eat beyond satiety. This will be critical in identifying novel therapeutic strategies for treating obesity with fewer side effects" concludes Dr. Borgland.

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Funding: Canadian Institutes of Health Research grant CIHR FDN-148473

Abstract:

**Synaptic alterations in the lateral OFC with diet induced obesity**

*Stephanie Borgland, University of Calgary*

The orbitofrontal cortex (OFC) receives sensory information about food and integrates these signals with expected outcomes. Thus, the OFC registers the current value of foods and updates actions based on this information. Our previous work demonstrated a decrease in GABA release probability onto pyramidal neurons of the OFC from obese rats. Because high fat diets alter endocannabinoid signalling, we tested the hypothesis that enhanced endocannabinoids alter GABA release probability in the OFC.

Rats were given restricted (1h /day), extended (23h/day) or no (chow only) access to a cafeteria diet. Whole cell patch clamp electrophysiology was used to assess alterations in local inhibitory synaptic transmission onto pyramidal neurons.

Rats became obese after 40- 45 days of extended, but not restricted access to a cafeteria diet. OFC pyramidal neurons from rats with extended access to a cafeteria diet had decreased inhibitory input partially due to an increase in endocannabinoid signaling at inhibitory synapses onto pyramidal neurons. Rats with extended access to a cafeteria diet exhibited increased endocannabinoid tone due to altered group 1 mGluR signaling. Obesity-induced changes in astrocytes in the OFC may contribute to these synaptic changes.

Taken together, these data suggest that cellular adaptations in the lateral OFC are associated with extended but not restricted access to a cafeteria diet. Thus, obesity can decrease inhibitory input to OFC pyramidal neurons which may underlie impaired food devaluation observed in obese rodents and humans.

Summary text

Giving unrestricted access to a high-fat, high-sugar “cafeteria-diet” to rats leads to obesity and to changes in a brain region called the orbitofrontal cortex, which integrates information about food and determines eating behaviour. These changes make food more attractive to rats, even when their hunger should be satisfied, explains Dr. Stephanie Borgland’s at the University of Calgary. These findings could lead to the identification of novel therapeutic strategies for treating obesity with fewer side effects.

Press release about a presentation at the Canadian Association for Neuroscience meeting by Freda Miller

Embargoed until May 15th, 2018, 7:00PM Pacific Time, 10PM Eastern Time

Title:

## Canadian researchers find key players for building and repairing the brain

Subtitle:

Understanding how the brain is built during development leads to new therapeutic approaches for repairing brain injury.

Text:

Research by Dr. Freda Miller and her team at the Hospital for Sick Children and the University of Toronto has determined how brain stem cells and the environment they live within collaborate to build brain circuits during development, discoveries that have led to a better understanding of neurodevelopmental disorders in children. The Miller lab and her basic research collaborators work closely with their clinical colleagues to harness this information and develop new approaches for treating brain injury. These results were presented at the 2018 Canadian Neuroscience Meeting, in Vancouver, May 15th, 2018.

During development, the mammalian brain starts life as nothing more than a collection of stem cells that then must generate the neurons and glial cells that form the complex network of connections required for proper brain functioning and cognition. One cause of neurodevelopmental disorders such as autism spectrum disorder is thought to be the failure of stem cells to correctly build the brain. Dr. Miller's team investigates how stem cells accomplish this task, and to understand how this process goes wrong in neurodevelopmental disorders. Since these same brain stem cells also persist into adulthood, this has led to the idea that it might be possible to manipulate these brain-resident stem cells to behave as they did during development, and in so doing to promote brain repair. Importantly, recent work from Dr. Miller and her collaborators suggests that this may indeed be the case, thereby identifying a new approach for treating the damaged or degenerating human brain.



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*“Neural stem cells are like "parent" cells that generate their children, the neurons and glia that build brain circuits, in a precisely controlled fashion in response to signals from their environment. These signals ensure that there are enough stem cells to build the brain, to make the correct amounts of neurons and glial cells at the right time and place in the developing brain, and that some stem cells persist into adulthood where they can participate in brain repair. If we can understand what these signals are, and how stem cells respond under normal circumstances, then that information will not only allow us to understand what happens in neurodevelopmental disorders such as autism spectrum disorder but will also provide us with the information we need to activate stem cells in the mature brain to promote repair"* says Freda Miller.

To understand brain stem cells and their environment, Dr. Miller is using approaches that range from stem cell biology to transcriptomics and proteomics that identify the proteins and RNA molecules that enable stem cells to build the brain and computational modeling, with the idea that understanding brain development and repair requires an interdisciplinary and highly collaborative approach.

*"The key to doing the best science is to ask big questions such as "how do you built functional brain circuits during development" or "how can you repair an injured brain" and then to seek out collaborators who are willing to work with you to answer those questions in an integrative and interdisciplinary fashion. This type of high-level collaboration is equally important when your discovery research unveils a potentially novel therapeutic strategy. This collaborative approach has been the key to all of our major discoveries"* says Freda Miller.

Summary text:

During brain development, neural stem cells generate the neurons and glial cells that form the complex network of connections required for proper brain functioning and cognition. Dr. Freda Miller's team in Toronto investigates how brain stem cells accomplish this task during development and seeks to understand why this goes wrong in neurodevelopmental disorders such as autism spectrum disorder. This information is also being harnessed to activate stem cells in the mature brain to promote repair.

Funding:

Canadian Institutes of Health Research, Stem Cell Network, Ontario Institute for Regenerative Medicine, and Howard Hughes Medical Institute.

Press release about a presentation at the Canadian Association for Neuroscience meeting by Brian MacVicar

Embargoed until May 16th, 2018, 10:15AM Pacific Time, 1:15 PM Eastern Time

Title:

## Stroke: Researchers shed light on the brain recovery process and new treatment strategies.

Subtitle:

Stroke is one of three leading causes of death in Canada and leads to permanent disability in about half of survivors. During an ischemic stroke, there is a blockage of blood flow which results in cell death in a specific area or the brain. Dr. Brian MacVicar and Dr. Louis-Philippe Bernier at the University of British Columbia have recently discovered how two types of cells, called astrocytes and pericytes, work together to regenerate blood flow in the areas affected by these strokes (called ischemic areas). These results were presented at the 2018 Canadian Neuroscience Meeting, in Vancouver, May 16th, 2018.

Astrocytes are a class of brain cells that are known to proliferate and become active following brain injury. The role of a second class of cells, called pericytes, was not known. Pericytes are known to regulate blood flow in the smallest blood vessels of the body, capillaries. Now Dr. MacVicar's team has shown that following stroke, pericytes also proliferate and migrate to the damaged area of the brain, inside a region that is bordered by astrocytes.

His team also showed that new blood vessels were formed at the interface between astrocytes and pericytes, in a wave that goes from the edge of the injured region towards the centre, thereby re-establishing blood flow in the region.

"Our results show that these two types of cell cooperate to re-establish blood flow in the injured region, and that within a few weeks, the area is fully vascularized, meaning that normal blood flow is restored. Additionally, we showed that the blood brain barrier is also re-established."

The blood-brain barrier is a protective mechanism that makes capillaries in the brain less permeable than blood vessels in the rest of the body, preventing the passage of bacteria and certain toxins that could be present in the blood, while allowing oxygen and nutrients to reach brain cells.

“Our work shows that pericytes are a dynamic population of cells in the brain, who become activated and proliferate in response to injury. This occurs through cross-talk between astrocytes and pericytes.”

The Heart and Stroke foundation of Canada indicates there are 62,000 strokes in Canada each year, and that 80% of people survive stroke. The Public Health Agency of Canada estimates that close to 742 000 Canadians live with the effects of stroke. A better understanding of the ways the brain can repair itself following stroke has the potential to lead to the identification of new targets for treatments to prevent damage or repair the brain.

-30-

Funding:

Abstract:

**Roles for astrocytes and pericytes in the regeneration of cerebral blood vessels after stroke**

Brian MacVicar, Djavad Mowafaghian Centre for Brain Health

The developmental maturation of cerebral blood vessels and the integrity of the blood-brain barrier (BBB) require the coordinated support from both pericytes and astrocytes. Astrocytes are known to proliferate and become reactive following stroke but the alterations in brain pericytes are unknown. Therefore we examined what roles brain pericytes play in repairing and restoring the cerebral microvasculature following CNS trauma and whether there are coordinated interactions with astrocytes. Following stroke, pericytes proliferate and migrate into the infarct region where they accumulate inside a border of reactive astrocytes. The pericyte-astrocyte interface forms an angiogenic zone that progressively migrates into the ischemic core, thereby supporting a wave of tissue revascularization. Within a few weeks normal vessels with an intact BBB are found perfusing the previously ischemic cortical area. Using single cell and population RNA

sequencing, we identify resting transcriptional signatures of pericyte subpopulations as well as a functional and transcriptional profile of activated pericytes following trauma. Brain pericytes in the adult brain represent a -major progenitor population that can modify their phenotype to contribute to the regeneration of cerebral blood vessels following injury in a process that recapitulates their role in developmental vasculogenesis. Our work defines a spatial and temporal coordination of the pericyte-astrocyte crosstalk that is critical in stroke recovery.

Summary

Dr. Brian MacVicar and Dr. Louis-Philippe Bernier at the University of British Columbia recently discovered how two types of cells, called astrocytes and pericytes, work together to regenerate blood flow in the brain areas affected by stroke. His studies show that both types of cells proliferate and get recruited to the edge of the damaged area. These findings have the potential to lead to the identification of new targets for treatments to prevent damage or repair the brain.



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Press release about a presentation at the Canadian Association for Neuroscience meeting by Fernanda De Felice

**Embargoed until May 16th, 2018, 3:15PM Pacific Time, 6:15 PM Eastern Time**

Title:

## Diabetes drugs show promise to treat symptoms of Alzheimer's disease.

Subtitle:

Discovery of a pathway linking Alzheimer's disease and Type 2 Diabetes leads to new strategies to preserve brain health.

Text:

Fernanda De Felice at Queen's University has discovered a disease mechanism common to Alzheimer's disease and Type 2 Diabetes. This mechanism, which consist of a pathway leading to inflammation in different parts of the brain, leads to glucose intolerance, memory impairments and degeneration of the connections between neurons, called synapses. This discovery can lead the way to new therapies to preserve brain health. These results were presented at the 2018 Canadian Neuroscience Meeting, in Vancouver, May 16$^{th}$, 2018.

Alzheimer's disease is a complex disorder. Health professionals and researchers are recognizing more and more that Alzheimer's disease affects more that just memory, as it also affects sleep, appetite, mood (often leading to depression). Compelling evidence indicates that brain regions not classically linked to memory are affected by this disease.

Alzheimer's disease and type 2 diabetes are both diseases whose prevalence is increasing worldwide. Studies have shown that Alzheimer's disease is a risk factor for type 2 diabetes, and vice-versa. Dr. De Felice and her team have therefore searched for common factors that could explain their co-occurrence.

"We know that the Alzheimer brain responds less to insulin, which is also indicative of some form of cross-talk in the pathways of these diseases. By looking at non memory-related symptoms of Alzheimer's disease we are getting a better understanding of the complex nature of this disease and of the different pathways it affects " says Dr. De Felice.

Her research on models of Alzheimer's disease, both in mice and non-human primates, has led to the identification of a pathway that causes inflammation in the brain, and that affects insulin signaling and endoplasmic reticulum stress. Reduction in insulin or insulin signaling is responsible for the increased blood glucose levels seen in diabetes, while endoplasmic reticulum stress is a measure of cell damage and can lead to cell death.

The molecular links between AD and diabetes suggests novel therapeutic strategies based on anti-diabetic agents. In previous work, Dr. De Felice's team had tested such a strategy, with the diabetes drug liraglutide. Her studies had shown that the drug could reverse cognitive impairment, changes in insulin sensitivity and restore synapses in non-human primate models of Alzheimer's disease.

"A better understanding of the pathway involved in the development of the complex symptoms of Alzheimer's disease will be key to identifying more therapeutic targets to treat this devastating disease and preserve brain health" says De Felice.

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**Funding:** Alzheimer's Society Canada, Weston Brain Institute, Canadian Institutes for Health Research (CIHR), National Institute for Translational Neuroscience (INNT/Brazil) and the Brazilian funding agencies Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) and Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ).

**Abstract:**

Fernanda G. De Felice | Queen's University
Molecular connections between Alzheimers disease and Type 2 diabetes

Neurodegenerative disorders linked to aging populations and unhealthy diets are emerging medical challenges worldwide, with increases in Alzheimer's disease (AD) and type 2 diabetes (T2D) of particular concern. Significantly, T2D is a risk factor for AD and vice versa, and studies have shown that AD and T2D are connected both in terms of cognitive failure and metabolic dysregulation. We have investigated pathogenic neurological mechanisms common to AD and T2D to determine the origin and impact of the brain metabolic stress in AD and to identify new targets for therapeutics that rescue cognition in AD. We described an inflammatory pathway that causes brain insulin signaling dysfunction

and endoplasmic reticulum stress in AD experimental models. Acting in the hypothalamus, this pathway leads to peripheral glucose intolerance. This same pathway acting in the hippocampus leads to synapse degeneration and memory impairment. These observations led us to actively investigate how specific hormones act in the brain to ameliorate metabolic stress and to prevent cognitive decline in AD models. The ultimate goal is to discover new strategies to preserve brain health.

Summary (75 words max)

Fernanda De Felice at Queen's University has discovered a disease mechanism common to Alzheimer's disease and Type 2 Diabetes. This mechanism, which consist of a pathway leading to inflammation in different parts of the brain, leads to glucose intolerance, memory impairments and degeneration of the connections between neurons, called synapses. This discovery can lead the way to new therapies to preserve brain health.