HEALTH SCIENCE INQUIRY

A publication platform for graduate students to discuss, discover, and inquire…

Volume 4 / Issue 1 / 2013

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Dialogue Piece

Main Submissions

Social, Economic, and Environmental Determinants of Mental Health and Addiction

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Cover Design

Two-Faced *(Detail)*

Darian Goldin Stahl

Description of Cover Design: The central theme for my art deals with the emotions that accompany living with a progressive disease like Multiple Sclerosis. I join internal MRI scans with impressions of body's surface to show how thoughts of impending disability are never far from one's mind. This piece portrays all the sides of one's face at once, which speaks to the dualism that occurs between the internal thoughts of disability and what is exposed to society. More universally, this print concerns what we all choose to show to the world, while being consumed by a hidden part of ourselves.

About the Artist: Darian Goldin Stahl began her printmaking career as an undergraduate at Indiana University Bloomington when she studied abroad in Venice, Italy, at the Scuola Internazionale di Graphica. Since then, she received her Bachelor of Fine Arts in Printmaking at Indiana, and then traveled to Canada to attend the University of Alberta and begin her Master of Fine Arts in Printmaking. She is currently working collaboratively with her sister, who is a PhD candidate in Bioethics at St. Louis University, and the two hope to perpetuate a culture of care and inclusion around people with disabilities at the intersection of art and science.

HEALTH SCIENCE INQUIRY TEAM

Call for Submissions (Issue #5. June 2014)

Health Science Inquiry will be publishing a new issue every year (June), and we welcome all Canadian graduate students to submit to us. We will be focusing on **Primary Healthcare** for our next issue, and although the full details are still being worked out, we will once again be partnering with a peer-reviewed journal and be implementing a similar competition for students. In addition to these structured commentaries, we will also be accepting news articles and creative editorial pieces for the next issue of Health Science Inquiry. If you're interested in writing a piece or have any questions about our next issue, visit our website (**www.healthscienceinquiry.ca**) or email (**healthscienceinquiry@gmail.com**)!

Special Thanks

Annals of Internal Medicine
Established in 1927 by the American College of Physicians

Journal of
MENTAL HEALTH

CJCMH / RCSMC
Canadian Journal of Community Mental Health

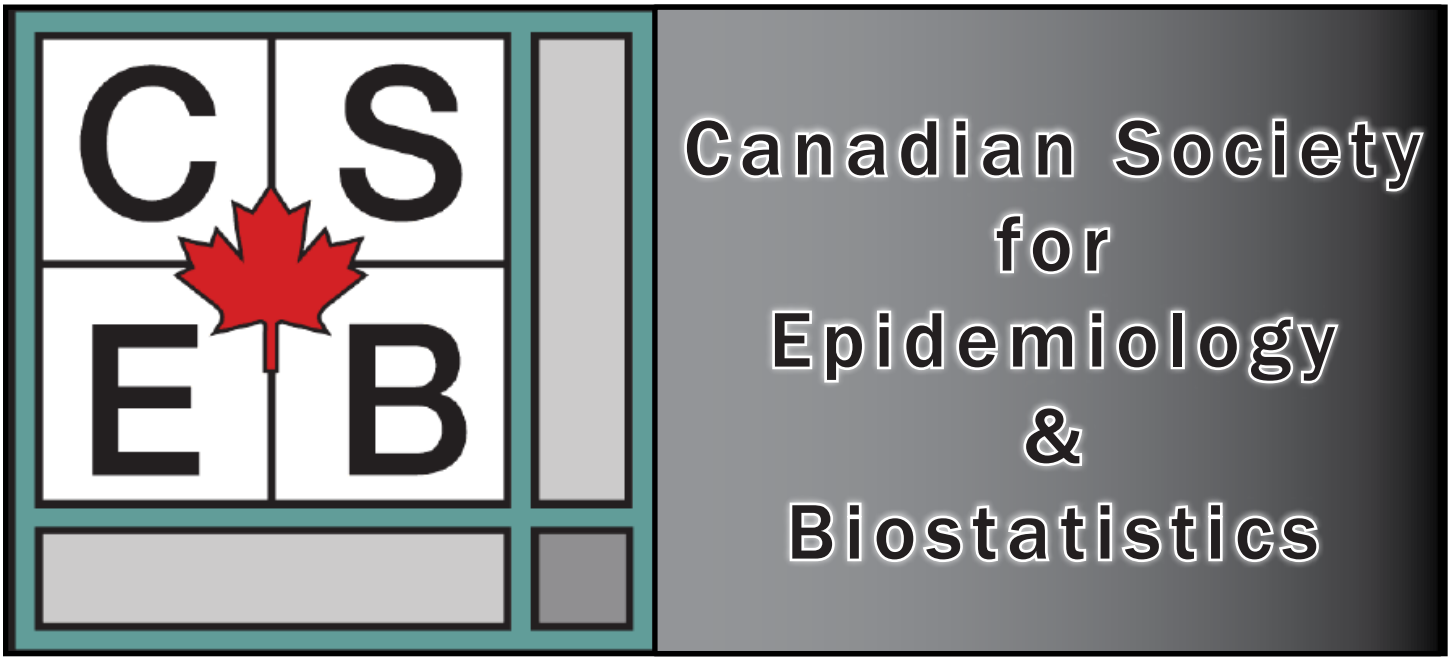
SPONSORSHIP

*This year, HSI will be donating **50%** of all sponsorship proceeds to Brain Canada, a charitable donation in the area of mental health and neurological disorders.*

Brain Canada

The charity we will be donating funds to this year is Brain Canada Foundation. 1 in 3 Canadians will be affected by a disease, disorder or injury of the brain, spinal cord or nervous system at some point in their lives. The Brain Canada Foundation is a national, charitable organization whose main goal is to fund research aimed at unlocking the mysteries of the brain. They will accomplish this by developing diagnostics, treatments, and ultimately cures, for brain disorders.

2013 Sponsors



INTRODUCTION

Letter from the Editor-in-Chief

Dear Readers

It's been another productive year at Health Science Inquiry (HSI) and I'm extremely happy to be able to present the 4th issue of our publication. Our theme this year is Mental Health and Neurological Diseases, which also marks HSI's first foray into the brain. In contrast to our previous issues covering a specific condition (H1N1, cancer, obesity/diabetes), our 2013 theme covers a range of diseases and topics, which will be evident in the pages to come.

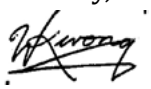
This issue starts off with a special introduction and historical timeline on psychiatry and psychology by Madelaine Gierc (HSI Proof Reader, 2012-2013). This introductory piece sets the stage for our regular News Articles and Artistic Images sections, as well as our Main Submissions. We were also lucky enough to have partnered with three academic journals this year – the *Annals of Internal Medicine*, the *Journal of Mental Health*, and the *Canadian Journal of Community Mental Health* – which ensured expedited review for the top article from each of our three submission categories. As always, we are indebted to our Faculty Judging Panel for taking the time to critique and select our top submissions.

2013 is also an opportune time for this year's theme, as the *American Psychiatric Association* will be releasing the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5). The release of the DSM-5 marks many changes to both the study and practice of psychiatry, and Diana Clarke – a statistician and epidemiologist from the *American Psychiatric Association* – provides an overview of this new release in one of our featured Discussion Pieces.

Outside of this journal, HSI is continuing its efforts to become a year-round platform for discussion through various initiatives. July 2013 marks the official launch of our revised website (www.healthscienceinquiry.ca), which will feature a regular Blog section managed by Megan Dodd (former HSI Managing Editor). This new blog will feature regular pieces written by Canadian graduate students throughout the year, and should offer readers meaningful perspectives on various issues in academia and science. In addition, Brienne McKenzie (HSI Managing Editor, 2012-2013) has launched a new sub-publication entitled *Spotlight on Careers*, which is a compilation of interviews and pieces delving into the subject of career prospects after graduation. This sub-publication is an excellent resource for any Canadian graduate student, and can be accessed and downloaded from our website.

It's been a very exciting year at HSI, and I am once again grateful of our dedicated team of staff members for their invaluable contributions. As HSI continues to grow as a student-run organization, I hope that this publication continues to incite discussion among your peers and colleagues. Enjoy!

Sincerely,



Wilson Kwong

Founding Editor-in-Chief

SPECIAL INTRODUCTION

Psychology, Neurology, and Scope: A Brief Orientation

Madelaine S. H. Gierc
Proof Reader (HSI 2012-2013)
MPH, PhD Student (Kinesiology)
University of Saskatchewan

"There is no health without mental health."
The World Health Organisation.

When you tell someone you're a psychology student, the most common response is: "So, are you analysing me?"

The polite response is to laugh and say "No," having already diagnosed the person with a bad sense of humour, a touch of paranoia, and a trace of naivety: it's not uncommon. Few non-psychologists realise that clinical psychology is just the tip of the iceberg. The common stereotypes – aloof therapist to evil government brainwashing – mask the richness of the field and what it means to study human thought.

In the broadest sense, psychology is the scientific study of behaviour and the mind, "behaviour" referring to observable actions, and "the mind" to processes like perception, cognition, and emotion. The area has interdisciplinary roots, most notably philosophy and theology, with early thinkers examining topics like materialism (e.g., Hobbes) and the soul (e.g., Descartes). The modern field is commonly dated to 1879 and the opening of the first experimental psychology laboratory in Germany; indeed, Wilhelm Wundt, the lab's founder, was the first person to be called a psychologist.[1,2] The past 134 years have been a time of rapid development, both in terms of knowledge base and research methodology. Today, common areas of study include neuropsychology, evolutionary psychology, developmental psychology, and social psychology.

Comparisons are frequently drawn between psychology and neuroscience, with neuroscience being depicted as more biology-driven. The mind is complex enough to necessitate such a split but, in reality, the distinction is largely arbitrary. The physical brain is, unquestionably, linked to behaviour, as is clearly displayed in case studies of brain injury patients.[c.f. 3] On the other hand, humans are far from static organisms: we are constantly changing, learning, and adapting to our surroundings. It is, therefore, unsurprising that environment, behaviour, and experience have the power to affect the physical structure of the brain. Striking examples include the effects of (a) culture on cognition[4] and (b) neglect on brain development.[5] However, even subtle aspects of everyday life – such as whether you work as a bus driver or a taxi driver[6] – have been linked to physiological changes.

The mind/body connection is emphasised by the field of behavioural medicine, as well as the realisation that health outcomes are linked to both psychological and psychosocial factors. Consider, for instance, that leading risk factors for chronic and noncommunicable disease – tobacco use, unsafe alcohol consumption, poor diet, and physical inactivity – are behavioural in nature.[7] However, behaviour can also be used as a mechanism for health promotion, disease prevention, and treatment. For example, not only is being active associated with positive physical and mental health,[8] but cognitive-behavioural strategies (e.g., self-monitoring and goal-setting) are effective tools for encouraging physical activity behaviour change.[9]

Mental illness, a pathological disruption in functioning, is a critical issue in its own right. Approximately 20% of Canadians will be affected by mental illness at some point in their lifetime; the remaining 80% will, undoubtedly, be indirectly affected via a family member, friend, or colleague.[10] Depression and anxiety are amongst the more common diagnoses, but the Diagnostic and Statistical Manual – the DSM – also specifies disorders like schizoaffective, dissociative identity, and ▶

primary hypersomnia. While variety is the rule rather than the exception, a key to many of the recognised disorders seems to be *excessiveness* of symptoms.

In addition to "classic" mental illness, it is also important to highlight the many neurological disorders. Alzheimer's disease and related dementias are amongst the most-discussed, and for good reason: they currently affect 500, 000 Canadians, and prevalence is expected to double by 2030 with significant economic and social implications.[11] However, there are also neurological birth defects (e.g., neural tube) and developmental disorders (e.g., autism spectrum); diagnoses like Parkinson's disease and multiple sclerosis; and physical damage, such as stroke or traumatic brain injury.

Psychology is very much a living field that is evolving and expanding, and it is directly linked to human health outcomes. But, beyond research, an equally important task is knowledge translation: applying what we know for both prevention and treatment. Mental *health* interventions (helping individuals realise their abilities and cope with normal life stressors[12]) are also of increasing interest. However, knowledge translation is not easy,[13] and mental health and mental illness are confounded by centuries of stigma, social taboo, and discrimination. Nonetheless, our work is essential. To echo the words of the World Health Organisation: there is no health without mental health. ■

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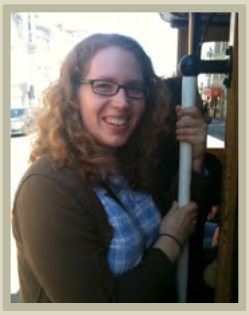


Madelaine Gierc

Madelaine is currently pursing a PhD (Kinesiology) at the University of Saskatchewan. Her research examines the psychosocial determinants of physical activity for health, with interests in sedentary behaviour, active living, and knowledge translation. She holds a BA (Psychology) from the University of Alberta and an MPH from Memorial University of Newfoundland.

SPECIAL INTRODUCTION

Psychology Timeline

A few of the many events in psychology and clinical psychology

Madelaine S. H. Gierc
Proof Reader (HSI 2012-2013)
MPH, PhD Student (Kinesiology)
University of Saskatchewan

1500 BCE
The first written description of the human brain appears in the Edwin Smith Papyrus.

c. 400 BCE
The era of Hippocrates, father of medicine. The four humors (blood, phlegm, black bile, and yellow bile) are hypothesised to play a role in determining personality. Mental illness is understood as a physical disease.

c. 387 BCE
Plato founds the *Academy*, a school of philosophy and science. He sees the body and soul as separate entities.

www.mathpath.org

120-201 AD
Galen works on a theory of personality and is the first to classify the emotions.

1247
The first western mental hospital, Bethlehem Royal Hospital ("Bedlam"), opens in London.

1637
Descartes publishes *Discourse on Method*, containing the famous: "I think, therefore I am."

c. 1650
Hobbes argues that mental processes are the result of the motion of brain atoms. He stresses the role of experience as the source of human knowledge.

c. 1770
Phillippe Pinel takes control of the Bicêtre asylum and forbids the use of chains and shackles. He removes patients from dungeons, provides them with sunny rooms, and allows them to exercise on the grounds.

www.nlm.nih.gov

c. 1790
Kant develops rationalism and empiricism. He argues that, while the mind has no substance, it is an active process that converts raw perceptions into ordered experiences.

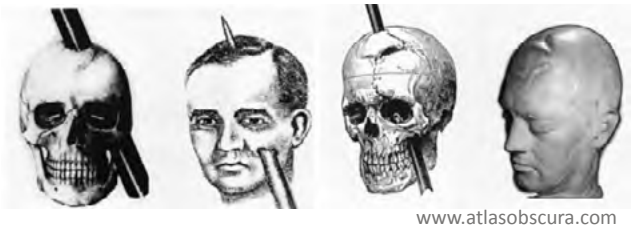
1838
The first psychology course is taught in Canada by Thomas McCulloch at Dalhousie University. ▶

DALHOUSIE UNIVERSITY
Inspiring Minds

www.dal.ca

1848

Phineas Gage survives a significant brain injury, but experiences considerable changes in his demeanor. It is the first case in which a direct link is drawn between brain damage and personality changes.



www.atlasobscura.com

1859

Darwin publishes *On the Origin of Species.*

1879

Wilhelm Wundt opens the first experimental psychology lab in Leipzig, Germany.

en.wikipedia.org

1880

Galton starts the systemic use of questionnaires.

1890

Charles Roy and Charles Sherrington show that brain activity is correlated to blood flow. Their research forms the basis of modern fMRI.

> "The subject to be observed lay on a delicately balanced table which could tip downwards either at the head or the foot if the weight of either end were increased. The moment emotional or intellectual activity began in the subject, down went the balance at the head-end, in consequence of the redistribution of blood in his system…"

1889

James Baldwin opens the first psychology laboratory in Canada.

1900

Freud publishes *The Interpretation of Dreams*. His work, such as the "talking cure," helps form the foundation of modern clinical psychology.

1901

Alois Alzheimer begins to work with Auguste D., a 51-year-old woman with strange behavioural symptoms and memory loss.

1905

Binet and Simon develop a scale to determine mental age, which is used to identify mental retardation in school children. Their work marks the start of standardised intelligence testing.

1906

Pavlov publishes his findings on classical conditioning.

1915

C. S. Myers coins the term "shell-shock" to describe the symptoms of severely traumatised soldiers.

1920

Independent psychology departments appear at McGill and the University of Toronto.

1926

Piaget publishes *The Language and Thought of the Child*, which examines cognitive functioning in children. His observations lead to the conclusion that children think differently than adults.

traveldisequilibrium.wordpress.com

1934

The Montreal Neurological Institute is established at McGill University; Montreal soon becomes a world leader in neuroscience research and training.

1939

The Canadian Psychological Association is established. ▶

1942
Carl Rogers develops patient-centred therapy

c. 1950
The first generation of anti-psychotic drugs are released. The drugs do not cure, but help to control symptoms.

1952
The first Diagnostic and Statistical Manual (DSM-I) is published.

1963
Milgram examines the relationship between obedience and authority. Results suggest that behaviour is affected by situational factors.

www.scientias.nl

1970s
Deinsitutionalisation, the process of closing asylums and integrating patients into the community, begins in Canada.

1970s
Research into neuroplasticity, the brain's ability to change, grows in popularity. Prior to this, it was widely believed that the brain was fixed throughout adulthood.

1980s
An estimated 33% of homeless people are considered mentally ill, the majority of them suffering from schizophrenia.

1990s
Development of modern neuroimaging techniques, such as the fMRI.

2000
Researchers finish mapping the human genome

c. 2000
The growth of the mental health movement occurs, with increased emphasis placed upon positive psychology and wellness.

2012
It is estimated that there are 86 billion neurons in the human brain.

2013
Publication of the DSM-5. ■

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ARTISTIC IMAGES

By collaborating with numerous talented students across the country, we are able to feature an Artistic Images section to showcase various artistic interpretations of healthcare and the medical sciences.

Artistic Images

Cara Mason

Cara Mason is a multidisciplinary artist and children's art educator from Winnipeg, Manitoba. Mason works to create visual representations of mental illness with her art. Her dark subject matter is balanced by delicate imagery in the hopes of drawing the viewer in and sparking a conversation about mental health. This is done with the use of painting, silkscreen, and photography. With these three mediums she creates figurative realism with elements of geometry to contrast the organic curves of the body.

Disorder (oil on canvas, 24"x36", 2013) is a series consisting of three different portraits of woman with mental illnesses [from top to bottom: Borderline Personality Disorder, Bipolar Disorder, and Obsessive Compulsive Disorder]. The paintings depict a moment in which someone suffering with mental health is trying to regain control over their condition. By painting varying illnesses in similar poses, Mason is exploring how despite differing diagnoses we all break down in the same way. When posing her subjects, Mason asked them to position themselves the way they do when having a break down. Often, people with mental illness have a default pose they use to comfort themselves and regain control. Despite the differing conditions the subjects all chose a fetal like position where they held themselves and created a barrier between the outside world and their body.

Artistic Images

Morning 2 . (Film Still)
Brad Necyk

One Too Many Mornings: Sleep Meds. (Photography)
Brad Necyk

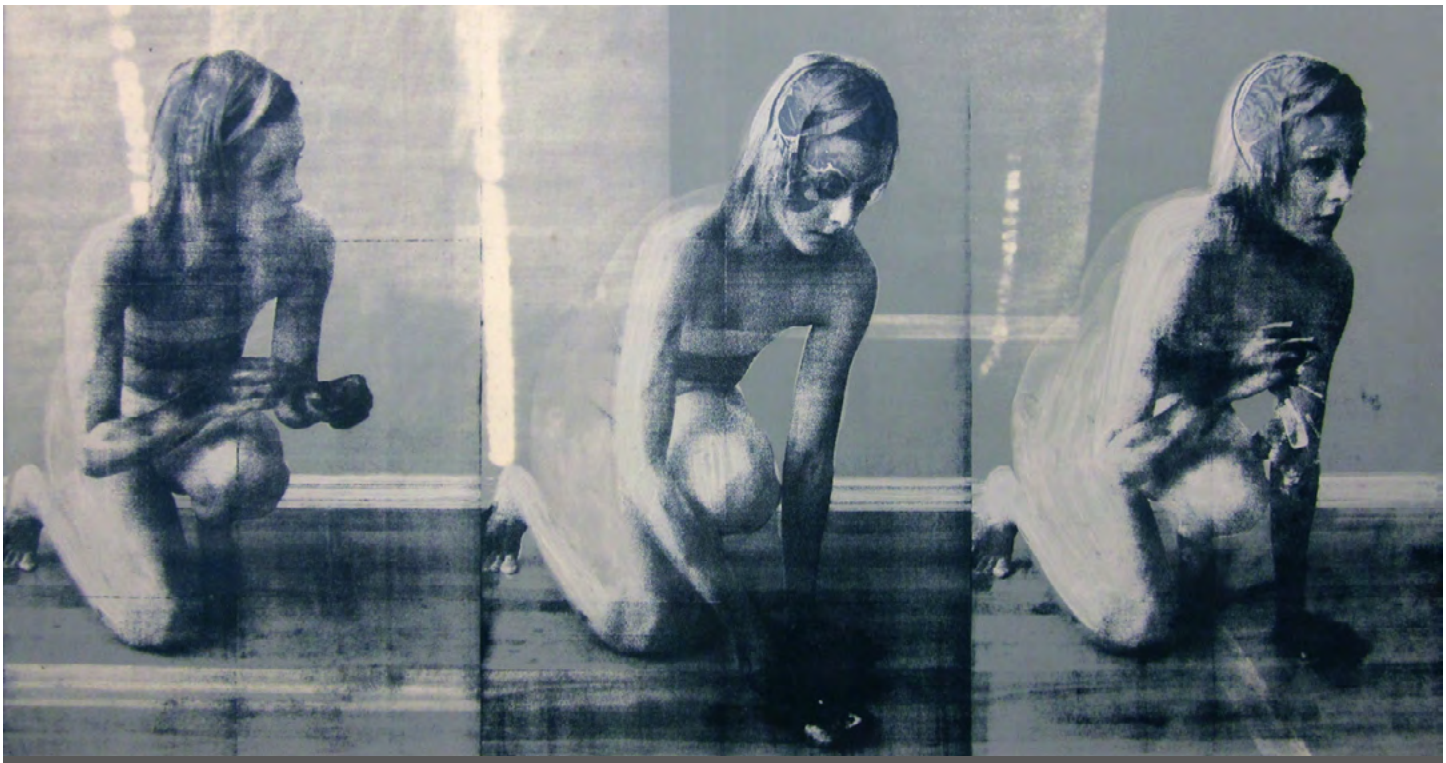
One Too Many Mornings: All Meds. (Photography)
Brad Necyk

Brad Necyk (bradnecyk.com) University of Alberta

Brad Necyk is an Edmonton based artist working within the mediums of photography, video and performance and exploring the intersection between the body and the administrative techniques of medicine, specifically psychiatry. He is currently working on his MFA at the University of Alberta in Drawing and Intermedia and teaches within the department. His work has been shown across Canada and he has delivered a number of academic papers across North America around pharmaceutics, psychiatry and art.

These photographic pieces are part of a large body of work looking at how the psychiatrist is able to gain access and penetrate the body – a complete anatomization of the body, installing sublimated substance into the central nervous system to metabolize and precisely bind to its structures and alter subjective experiences. These works in particular function alongside audio that either is describing the statistical occurrence of various adverse events from the application of these psychoactive medications or the subjective experiences that are altered by them. They tie into the Greek notion of the Pharmakon as simultaneously a remedy and a poison, while on a larger scale working within the Immunitary paradigm of Biopolitics. The Biopolitical administration to populations through enhanced medical application to prolong life is intensified within psychiatric administration, as you are not simply statistically prolonging life but seizing the abject, the abnormal and the unproductive, treating and normalizing behavior, ultimately returning them as functioning and working individuals.

Artistic Images



Dropping Keys (Print)
Darian Goldin Stahl

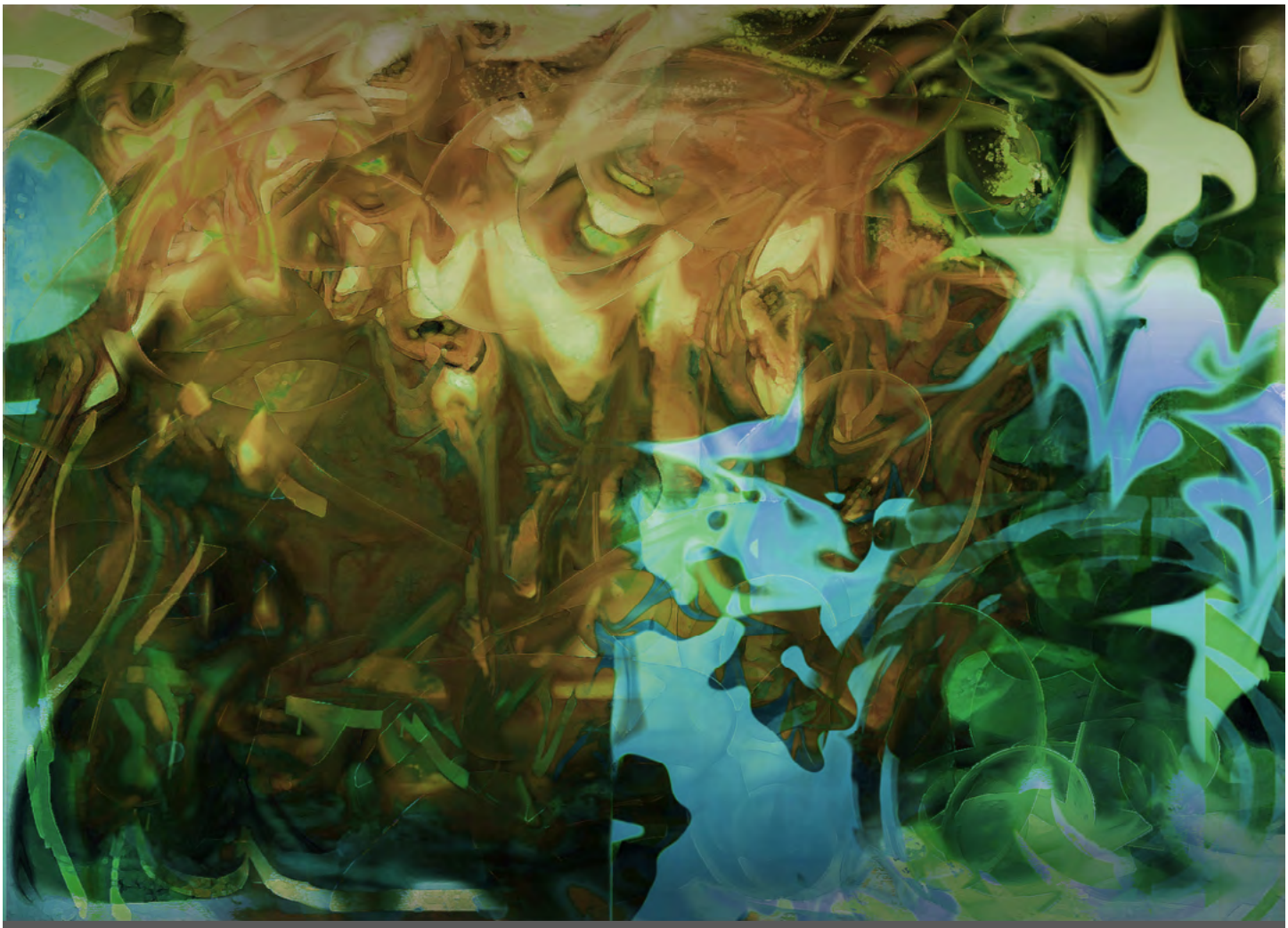
Darian Goldin Stahl
University of Alberta

Dropping Keys: This piece was inspired by the writings of Stahl's sister, who has Multiple Sclerosis, and what it is like to living with a progressive disease. Stahl's sister explains that when she drops her keys, she is unsure if she is just being clumsy or if she is experiencing a relapse. In this print, the figure is being followed by light columns that appear on the wall due to the morning sun shining through the window shades. These columns recall the bright abnormalities that appear on MRI scans. Further, Stahl has literally incorporated the MRI scans of her sister's brain as well. Ultimately, it is Stahl's goal to use these metaphors for disability to give the viewer a glimpse of what it is like to live with dis-ease.

Numb: In this silkscreen print, Stahl has frozen a figure in a block of ice to raise concerns of mobility and functionality with a numb body. This piece was inspired by Stahl's sister, who has the progressive disease Multiple Sclerosis. Stahl is interested in ways of portraying disability without the use of artifice, such as a cane or wheelchair. Overall, this print is about the uncertainty of one's future with an ever-failing body.

Numb (Print)
Darian Goldin Stahl

Artistic Images



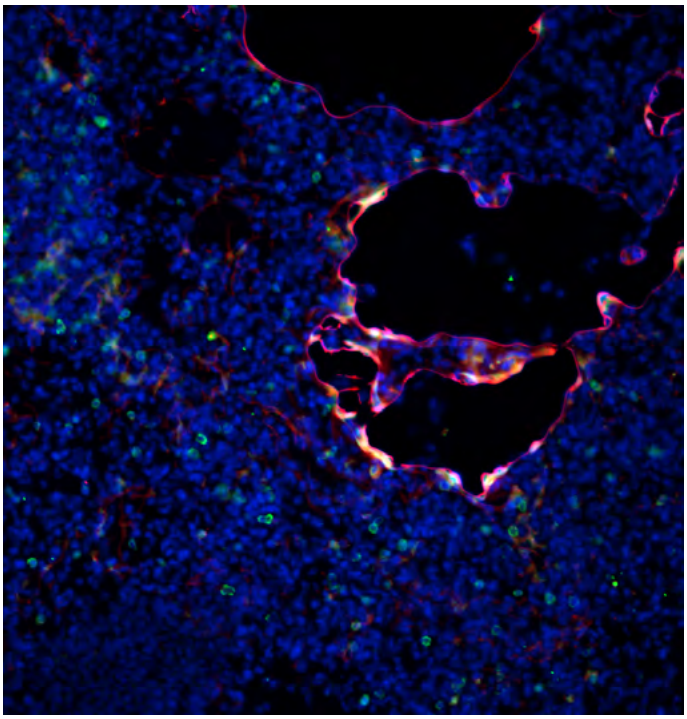
Grin and Bear It. (Manipulated digital photographs)
Karen Edwards.

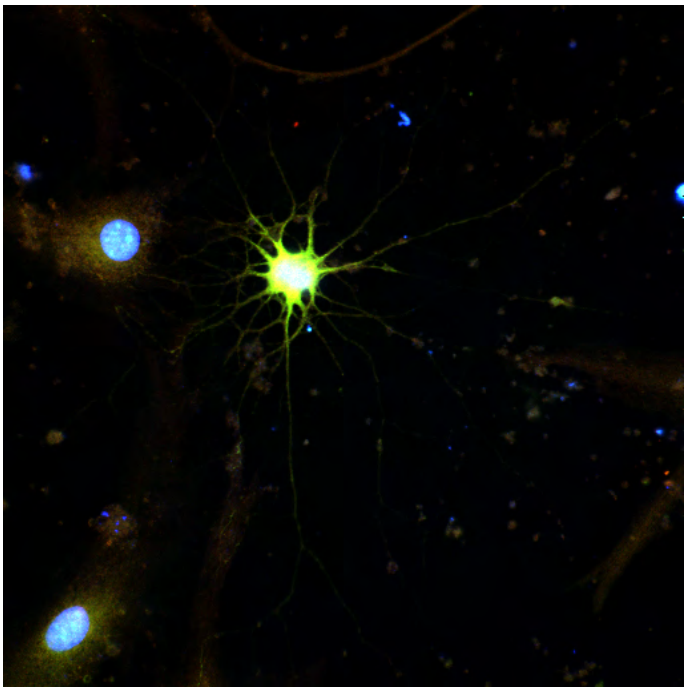
Karen Edwards (www.karenleeedwards.com)
University of Manitoba

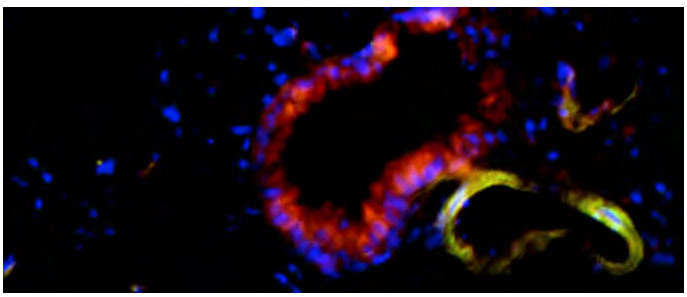
Karen Edwards is a multi-disciplinary contemporary artist. She obtained her B.F.A. degree, at the School of Art at the University of Manitoba. Currently, the focus of her processed based practice deals with the deconstruction and reconstruction of an issue she finds to be of importance. Working unconsciously, through the genius that whispers in her ear, the results are unexpected and curious. The images lie in waiting for the viewer's imagination to conjure up their own story.

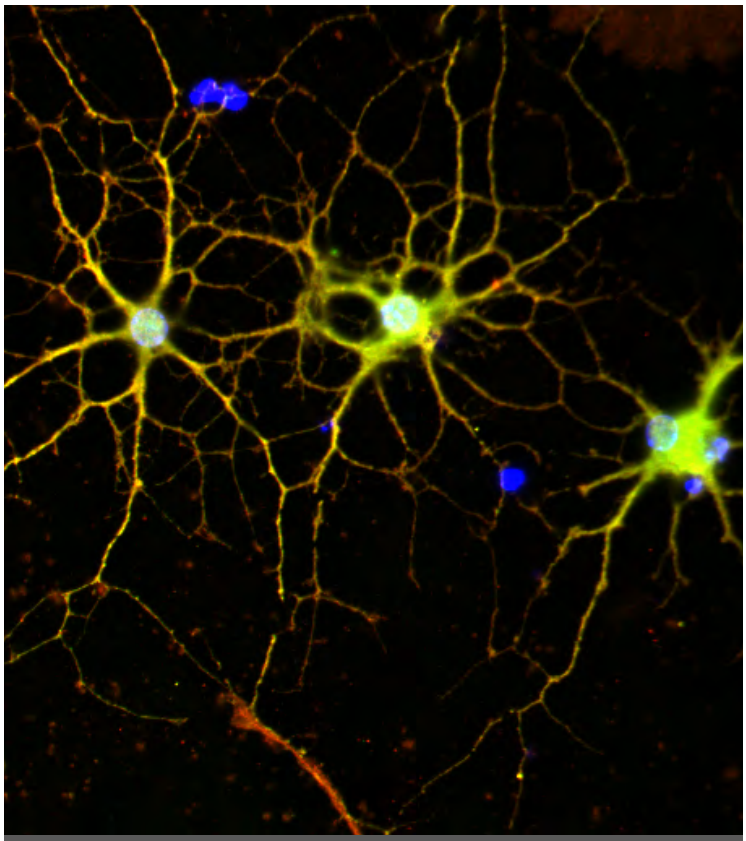
Being a process oriented artist, when she reacts physically to an issue, she gets to work. While making this print, *Grin and Bear It*, she was dealing with an event between her Alzheimer affected mother and herself. Karen cannot even imagine what this former strong minded woman is going through. This print is the resolution of the event. Within the layers there are very few shapes that are recognizable. The abstract forms speak to the confused world of an Alzheimer patient. There is the illusion of a person in the top middle of the painting which represents both her mother, during her lucid moments, and Karen, in her non-lucid moments.

Artistic Images









Stem cell derived oligodendrocytes that have been differentiated in vitro. Processes are searching for unmyelinated neurons (Microscopic images)
Katherine Ludlow and Josef Buttieg

Dr. Josef Buttigieg and Katherine Ludlow

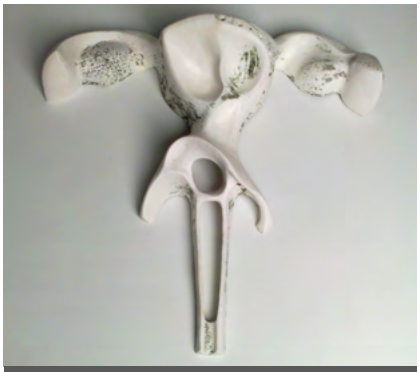
University of Regina

Dr. Josef Buttigieg is a stem cell biologist studying neuronal development and regenerative medicine. These are images of some stem cells that his lab works on. His research focuses on remyelination after spinal cord injury and myelination of the nervous system during development and disease (e.g. at birth, schizophrenia, or multiple sclerosis).

Katherine Ludlow is currently pursuing a MSc degree under the supervision of Dr. Buttigieg in Biology at the University of Regina. Her research interests include neural stem cell physiology, specifically related to factors involved in myelination by olidodendrocytes in the central nervous system.

Artistic Images

Adapt (Slipcast Cone 7; Porcelainious Stoneware)
Loricia Matheson



Adjust (Press Molded; Paper Clay; Cone 06)
Loricia Matheson

Overcome (Press Molded; Paper Clay; Cone 9)
Loricia Matheson

Loricia Matheson University of Manitoba

Loricia Matheson is currently in her second year of Fine Arts at the University of Manitoba. She is 45 and a single mother who has faced a long road of personal, emotional, physical and financial challenges. She is looking at attaining a degree in ceramics and currently taking psychology.

Matheson was raised by a single parent who was widowed at 18 and despite her mother's situation, provided for her and her brother. Matheson (at 23) had her first born child who remained in a Pediatric Intensive Care Unit until the age of two. Her daughter still required 24 hour nursing care until she was 15.

She faced the difficult choice of ending her 12 year marriage after enduring various forms of abuse and ongoing infidelities. In 2008 when her mother was diagnosed with cancer for the second time, she was accused of kidnapping her two youngest children when she took them out of the province to see her mother. Although she has been separated for 10 years, she is still fighting for access to her daughters. She has spent a decade dealing with the government, an angry ex, and judicial systems.

Even though it means student loans and the unknown, at this stage of her life, she envisions her work acting as a springboard, to enlighten others; a means to exemplify those who have endured; found strength to Overcome, Adjust, and Adapt.

Matheson has returned to school because she wants to continue to take classes that will hone the skills as an Artist, survivor and educator. Her aim is to continuing with classes in violence's and criminology, producing work that will be challenge social and cultural conventions, while empowering victims of violence.

There is an underlying theme of spirituality that informs her practice. Inspiration comes from the female form and from within. The figure inspires her with organic lines, voluptuous curves, natural growth in pattern and evolution. This is why she is attracted to the form – its' iconography, and history in art, culture and fantasy.

There are many ways to interpret mythologies, symbolism and the body. The malleability of clay allows her to rediscover her past, this present and the future, while speaking of a contemporary language of volume, shape and space.

Matheson intends to refashion form through modification and fracture notions of individuality. Using the concept of multiples; she will explores portions, shape, natural and manmade elements to conceive new life.

Thinking conceptually, creating sculpture/objects that reference symbolism, while incorporating components that may or may not relate to each other specifically. Matheson wishes to engage the viewer in an experience that is both positive and negative. The observers experience will contribute to the works contemporary meaning and enhance the emotional concept of the pieces.

Matheson has a strong belief in a higher power and that we are guided by what is right and wrong. She believes we make choices that are influenced by both what we carry internally and are influenced by externally. Her motto, "By staying true to myself, I have Overcome adversity, Adjusted to circumstances and Adapted (resurgence)."

SECTION 1: NEWS ARTICLES

News Reporters from HSI's Editorial Team investigated various issues in Mental Health and Neurological Disorders to present readers with insight into the latest research and initiatives across the country. Our team of reporters conducted research and interviews with key experts in a range of different topics.

News Article

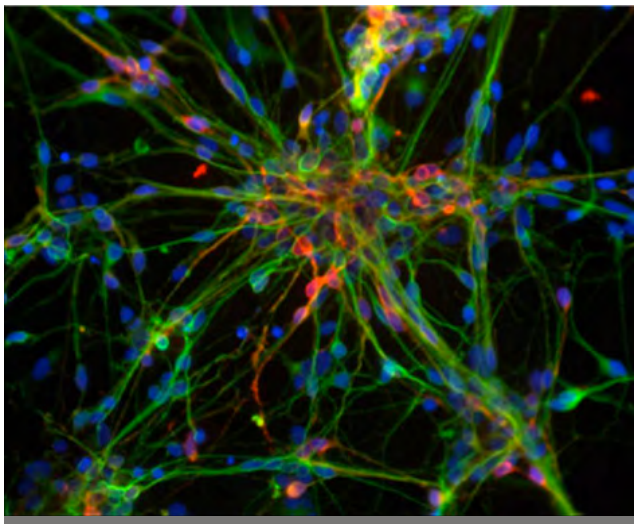
Stem cells and neurogenesis: Implications in the pathogenesis and Treatment of Alzheimer's Disease

Winnie Ng *(University of Toronto)*
News Reporter (HSI 2012-2013)

Alzheimer's disease (AD) is the most common form of dementia and is primarily characterized by learning, memory, and cognitive loss due to initial neuronal cell death in the hippocampus that spreads to other areas of the cerebral cortex and is eventually fatal. AD is progressive and irreversible. Presently there is no cure, and many of the available treatments only aim to modify the course of disease. According to the Alzheimer Society of Canada, dementia currently affects approximately 500,000 Canadians; however, this number is projected to more than double by 2038. The economic burden of dementia in Canada was upwards of 8 billion dollars in direct health costs in 2008, with an additional 1.8 billion dollars for indirect costs such as lost wages and decreases in the labour productivity of patients and caregivers.[1] Moreover, this does not account for the physical and emotional burden of AD for family members and other caregivers who witness the effects of cognitive decline. Clearly, effective strategies are needed that support all individuals affected by AD, and significantly more research is needed to develop and test novel treatments that may mitigate its effects or lead to the development of a cure.

"[M]ore research is needed to develop and test novel treatments that may mitigate its effects or lead to the development of a cure."

Age is one of the most important risk factors for AD, although AD is not necessarily a disease of ageing, as previously believed. It was over a century ago that Dr. Alois Alzheimer found plaques and tangles in the brain of a patient with 'senile dementia' and these markers have become hallmarks for the diagnosis of AD.[2] Plaques refers to beta amyloid plaques that are comprised of beta amyloid protein (Aβ) produced from the cleavage of amyloid precursor protein (APP), whereas tangles refers to neurofibrillary tangles that form due to tau protein aggregates.[3] However,



The discovery of adult neuronal stem cells in mice by Reynolds and Weiss at the University of Alberta has opened up the possibilities for neurogenesis as a potential treatment in response to neural injury.[6] *(Flickr: Science3point0.com)*

beta amyloid protein and tau protein have been observed in humans post-mortem without AD dementia,[4] indicating that these proteins may be necessary but insufficient to induce AD. Nevertheless, most AD research has focused on investigating the pathogenesis of AD in the context of the plaques and tangles.

Stem cells have become a very exciting area of regenerative medicine since the discovery of human embryonic stem cells in 1998.[5] The inherent characteristics of stem cells, having a high capacity for self renewal and the ability to differentiate into various cell types, provides the potential for a unique opportunity to treat diseases that require regeneration or replacement of damaged cellular tissue. Neurons were primarily considered a terminally differentiated cell type, meaning that these specialized cells could not regenerate themselves. However, the discovery of adult neuronal stem cells in mice by Reynolds and Weiss at the University of Alberta has opened up the possibilities for neurogenesis as a potential treatment in response to neural injury.[6] More recently, Fernandes *et al.* discovered that neuronal cells could be generated from skin-derived precursors found in the dermis,[7] which extends the potential for autologous stem cell transplantation in the treatment of neurological disorders. ▶

Dr. Karl Fernandes, an assistant professor in the Department of Pathology and Cell Biology at the Université de Montreal and the Canada Research Chair in Stem Cell Neurobiology, is taking an alternative approach to studying AD and investigating how the biology of stem cells is affected by neurological diseases such as AD and how they could be involved with the pathology. "Neuronal stem cells (NSCs) are involved in all four major areas of neuroscience; including how the brain was built, how it works, what happens when it breaks down, and how to fix it," says Dr. Fernandes, which demonstrates why it is such a good candidate to study in the context of neurological diseases.

Since AD is very difficult to study in humans, animal models of AD have been useful to study the mechanisms of AD. One such model is the triple-transgenic mouse model 3xTg, which in short is a $PS1_{M146V}$ knock-in mouse that contains the human APP_{Swe} and human tau_{P301L} transgenes that results in the development of the hallmark plaques and tangles observed in AD pathology.[8] Using this model, Dr. Fernandes' research group found that 3xTg mice had decreased neurogenesis in the hippocampus and subventricular zones through BrdU and Ki-67 labelling as compared to the wild-type mice, and this was associated with decreased cognitive function.[9] Moreover, this down regulation in neurogenesis in the 3xTg mice was similar to what was observed in the wild-type mice at an older age. What is more interesting is that the decrease in neurogenesis in the 3xTg mice preceded the development of the hallmark plaques and tangles of AD. These findings are intriguing as it shows changes in the NSC population in an AD-like environment and suggests that the breakdown of neurogenesis may be implicated in the pathology of AD. On the other hand, these findings do not rule out that AD pathology may lead to the decrease in neurogenesis.

"If activation of stem cells is increased in the hippocampus it may increase cognitive function as a whole, independent of whether we get the disease or not."
Dr. Fernandes

It must be cautioned that it is unknown whether the AD pathology in animals is truly representative of what occurs in humans. Thus, it questions the relevancy of animal models. However, in humans only an endpoint snapshot can be obtained of AD. There are many animal models of AD; this particular 3xTg mouse model is unique in that it reproduces the AD environment with regards to both the plaques and tangles. Although questions still remain about whether these results are translatable to humans, according to Dr. Fernandes the first step is to see whether these findings can be translated to other AD models. In terms of the big picture, "the implications of this research are that decreased neurogenesis at an earlier time point may accelerate cognitive defects," says Dr. Fernandes and, "if activation of stem cells is increased in the hippocampus it may increase cognitive function as a whole, independent of whether we get the disease or not." Presently neurogenesis cannot be measured in humans, although the technology is getting close. Based on current research, it is more likely that any clinical approach would involve modifying the course of AD rather than developing a cure. Transplantation of NSCs is also, as of yet, unlikely as there are still concerns whether proper neurons and connections will develop or whether NSCs will provide trophic support rather than neuronal replacement. One area of promise may be to stimulate neurogenesis from endogenous NSCs to treat AD using drugs already available on the market that may activate specific pathways required by stem cells for recruitment and/or differentiation; as was found with thediabetes drug metformin, which increased neurogenesis and enhanced cognitive function in mice via the atypical protein kinase C-CBP transcriptional co-activator (aPKC-CBP) pathway.[10]

Perhaps the most profound implications are that studying the biology of NSCs, rather than focusing strictly on its potential as a treatment, may help to understand and even prevent debilitating neurological diseases in the future and many of these findings could be translatable between stem cell fields. Stem cell research has been dominated by Canadian innovation since their discovery by Till and McCullough in the 1960s and foundations like the Stem Cell Network continue to support Canadian researchers to further fuel the enormous potential for stem cells to improve and advance human health. ■

Acknowledgements

Special thanks to Dr. Fernandes for his contribution to this news article.

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Winnie Ng

Winnie Ng completed her B.Sc. in Biomedical Toxicology at the University of Guelph and is currently finishing her Ph.D. at the University of Toronto in the Department of Pharmaceutical Sciences. Her thesis research focuses on the mechanisms of idiosyncratic drug reactions and involves testing the immunological changes induced by aromatic amine drugs in animal models. Upon completion of her doctorate degree, she hopes to maintain a similar path and pursue a career in drug safety. She is also actively involved in the Life Sciences Career Development Society and enjoys teaching others about science as a Let's Talk Science volunteer. In her spare time she likes to be outdoors exploring new trails, travelling, learning about new cultures, and she is also fascinated with the Group of Seven artwork.

News Article

Alberta's call for collaboration in Mental Health Capacity Building

Stephanie Patricia Kowal
(University of Alberta)
News Reporter (HSI 2012-2013)

Mental health conditions impact an enormous proportion of Canada's population. One third of Canadians experience mental health problems at some point in their lives and one in five Canadians will experience a mental health condition within the next year.[1] Such diagnoses include, but are not limited to, anxiety, depression, schizophrenia, and bi-polar disorder. These types of conditions can cause major changes in a person's thinking, emotional state and behaviour, and disrupt the person's ability to work and carry on their usual personal relationships. Mental health conditions are especially concerning in children and youth because research shows that half of all lifetime cases of mental illness begin by age 14.[2]

Even though mental health problems are so pervasive in Canada, many people do not receive professional mental health care. If they do decide to seek help, people often visit their family doctor or other primary health care provider who may not have the knowledge, skills, or time to provide mental health care.[3] Furthermore, consumers may not access, or be able to access, their full range of mental health services because they, or the general physician, are not effectively coordinated with mental health care providers.[3, 4]

"The objective of The Way In *is to provide mental health promotion and prevention strategies and tools to students at under-served junior high schools."*

To begin addressing the mental health burden in Alberta, in 2008 the provincial government began funding interdisciplinary and inter-sectorial mental health initiatives as part of the *Children's Mental Health Plan* for Alberta. A coordinated and collaborative approach to optimizing the mental health and well-being of infants, children, and youth drives the function of this plan. Under this action plan, the province implemented the further focused *Mental Health Capacity Building Project*. This initiative aimed to establish projects that followed collaborative approaches to provide the staffing and support required to implement integrated, school-based community mental health promotion, prevention, and early intervention programs. The projects are developed locally and are coordinated and implemented through partnerships between Alberta Health Services, school jurisdictions, parents, community agencies, and other regional service providers.

TWI uses schools as a gateway for offering wider service availability to traditionally under-served youth. This localizes services within the schools, where previously, the nearest mental health service providers were across the city. *(www.instituteoffamilies.ca)*

The Way In initiative is one such program which has been very successful in following the collaborative model while effectively addressing the mental health needs of youth in Edmonton, Alberta. The objective of *The Way In* (TWI) is to provide mental health promotion and prevention strategies and tools to students at under-served junior high schools. The end goal of the project is to build mental health capacity within the schools and to reduce stigma around mental health conditions. TWI uses schools as a gateway for offering wider service availability to traditionally under-served youth. This localizes services within the schools, where previously, the nearest mental health service providers were across the city. These types of referrals are generally infeasible for families using public transportation or living under extremely tight time constraints due to multiple jobs, education attendance, or childcare requirements. ▶

News Article

TWI serves mental health needs that run the gamut of concerns including addiction, bullying, mentorship, academic issues, social skills, and self-esteem. To address all of these mental health needs, TWI operates under 10 paid employees and over a dozen community and government partners. The employees include: three full time success coaches in schools to provide mental health supports through universal, targeted, and individual programming; a registered nurse for mental health assessments and support; an addictions counselor; a mentorship coach who creates individual and group mentoring programs based on student needs; an Aboriginal commitment coach in each school who focuses on the access and support needs of Aboriginal students and their families; and a project coordinator. The organizational partners include different governmental offices, various community organizations, family centres, Big Brothers and Sisters, and Edmonton Public Schools, among others.

> *"[S]uccess and sustainability of [TWI] hinges on the volume and intensity of these partnerships [different governmental offices, various community organizations, family centres, Big Brothers and Sisters, and Edmonton Public Schools, among others]. The collaborative process among all of these partners creates conditions that facilitate a high social return on investment."*
> **Jennifer Parenteau**

Jennifer Parenteau, TWI's program coordinator, explained that the success and sustainability of the initiative hinges on the volume and intensity of these partnerships. The collaborative process among all of these partners creates conditions that facilitate a high social return on investment. To coordinate a highly efficient mental health response, TWI uses a *wrap-around model* of service delivery. This model strives to provide accurate services in an efficient manner, rather than overload youth with services provided by multiple doctors and organizations. With a wrap-around model, the services are inside the school and available to every student that may need it. Ms. Parenteau was proud of TWI's ability to provide coordinated in school service delivery which ensures short wait times to meet with community agents. In addition, the location of the services means that the councillors and coaches have a constant daily presence so they can connect with people regardless of the magnitude of the students' needs.

Most importantly, this partnership network of service providers, teachers, administrators, and community members provide mental health services to individual students while keeping everyone up-to-date on the needs and progress of each child. This type of location-based collaboration eliminates the risk of siloed services miscommunicating (or not communicating at all) about what has (not) been provided for students. In turn, such collaboration can meet the holistic needs of individual children.

For TWI, an important part of the initiative is the ability to follow-up on child's well-being across different schools and years. Ms. Parenteau stated, "A lot of the time people drop the ball on kids. If a kid moves across the city and we know the kid was seeing a therapist [when they were at one of our schools], we will contact the school to see what types of services it offers. We call the parents to tell them what's available in their community for their children, and we follow-up to see if the kid has seen a therapist since they arrived in the new school. We're not dropping the ball on kids."

As with many health promotion and prevention programs, TWI's biggest challenge is maintaining funding. They need funding to sustain positions not under the *Mental Health Capacity Building project*. For this reason partnerships that offer in-kind staff and support have become incredibly important. For example, TWI contracts three success coaches and an aboriginal commitment coach from a ▶

This partnership network of service providers, teachers, administrators, and community members provide mental health services to individual students while keeping everyone up-to-date on the needs and progress of each child. *(Flickr: aapne jf)*

local family centre, and in return that family centre donates an in-kind family support worker full time. These types of contributions are essential to keep the wrap-around services operational and feasible. Funding becomes confusing when different positions are funded through different agencies but it is incredibly important because this process facilitates partnership-building. Without these challenges, TWI would not be driven to create the in-kind networks and coordinated knowledge that has been fundamental to their success as a youth mental health initiative. ■

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Stephanie Patricia Kowal

Stephanie is currently a student in the School of Public Health at the University of Alberta. Her thesis work comprises a community-based research project aimed at understanding how new immigrant mothers in Edmonton, Alberta make immunization decisions for themselves and their children. With the findings, she and her research partners will create information content and delivery strategies that better suit the cultural needs and day-to-day realities of different immigrant communities.

News Article

Finding hope in Bill C-300: A call to action on suicide prevention in Canada

Nathaniel Pollock
(Memorial University)
News Reporter (HSI 2012-2013)

Harold Albrecht thinks it's time to change the way we think about suicide in Canada. In 2010, the Kitchener-Conestoga Member of Parliament received an alarming email from a constituent, informing him that three students from three different schools in his riding had died by suicide during a single week. The email concluded simply: "We need help."

> *"We are one of the only developed countries that does not have a federal framework or strategy to give resources and up-to-date stats to the groups that are already on the front lines."*
> **Harold Albrecht**

For Albrecht, this was a call to action from a community in crisis. In response, he began speaking publicly about suicide, in his riding, and in Parliament. When he did so, Albrecht said, "Colleagues and others in the community started approaching me with their stories." He quickly learned about the stigma that often prevents families from asking for help when someone is suicidal. Albrecht realized that suicide has a bigger impact than he had ever imagined. Each year, suicide claims the lives of nearly 4,000 Canadians. In 2009, it was the second leading cause of death among youth aged 15 to 24 years old,[1] yet its place in our society is seldom openly discussed.

Conversations about suicide are not only socially taboo, but also largely off-radar for Canadian policy makers. "We are one of the only developed countries that does not have a federal framework or strategy to give resources and up-to-date stats to the groups that are already on the front lines," says Albrecht. In 2011, he attempted to correct this by introducing a private member's bill. Bill C-300 seeks to make policy changes that promote access to statistics about suicide and make it easier for communities and service providers to share best practices in prevention. With these changes, the MP also wants to spark a public dialogue about the issue.

Bill C-300 seeks to make policy changes that promote access to statistics about suicide and make it easier for communities and service providers to share best practices in prevention. *(Library of Parliament - Roy Grogan)*

Albrecht is not alone in his efforts to draw attention to suicide, nor is he the first to call for a national prevention strategy. For the last decade, the Canadian Association for Suicide Prevention (CASP) has lobbied for the political support that Bill C-300 has recently helped mobilize. In 2004, CASP released a report with specific recommendations for suicide prevention policy, clinical services, and public education.[2] This report was highly regarded by advocates, and it even helped shape national strategies in other countries.

According to CASP president Dammy Damstrom-Albach, there has been no political uptake of the report's recommendations at a federal level until now, and while CASP celebrates Bill C-300 as an important step, the proposal still has limitations.[3] When it reached the parliamentary standing committee, CASP and the Canadian Psychiatric Association proposed multiple amendments to the bill.[4,5] These changes were intended to tie comprehensive and actionable goals to the bill and align the legislation's structure with the recommendations from CASP's report. The proposed revisions included creating a coordinating body and setting targets for improvements to mental health care, suicide information systems, and public awareness.[4] "We are going to have to do some things to give [the bill] legs," Damstrom-Albach says, but despite CASP's efforts, none of the proposed amendments were adopted.[3] It seems that the gap between what ▶

advocates want and what Albrecht put forward may come down, at least in part, to money.

One of Canada's leading suicide researchers, University of Western Ontario's Dr. Paul Links, acknowledges that the systemic changes needed to reduce suicide rates require financial commitments beyond the scope of the bill. "It's certainly a step forward," he says, "but it wouldn't create what is understood as a national strategy. It's not comprehensive enough." Dr. Links is unequivocal about the need for a federal strategy, though he believes that the government has been slow to act because it views health services as a provincial responsibility.

> *"[Bill C-300 is] certainly a step forward, but it wouldn't create what is understood as a national strategy. It's not comprehensive enough."*
> **Dr. Links**

Wherever the bureaucratic obligation lies, there is a role for the federal government to play in suicide prevention. Dr. Links notes that this is especially evident considering that Canada, not the provinces, is responsible for delivering health care federal prison inmates and some aboriginal populations. As it happens, males in both groups experience a disproportionate burden from suicide with rates between 5 to 10 times higher than in the general population.[6,7] Prisoners and some aboriginal communities also have high rates of mental health problems,[8,9] which are strongly associated with suicide.[10]

This known connection between mental illness and suicide risk is emphasized not only in CASP's report, but also in the Mental Health Commission of Canada's strategy, *Changing Directions, Changing Lives*. Both organizations have called for earlier detection and treatment of mental illnesses, and efforts to reduce the stigma surrounding mental illness. Given this overlap and the federal commitment to the Commission, it might be worth considering whether a distinct suicide prevention strategy is needed at all.

Albrecht accepts the criticisms of his bill's limitations, but explains that by its very nature, a private member's bill cannot commit government funding. For this, he is unapologetic: his priority has been to kick-start a public conversation and to create a bill that can garner support from both the government and the opposition to create a distinct strategy.

Albrecht also remains hopeful about what Bill C-300 can accomplish. "The conversation is as important as the legislation itself," he says. "There is a stigma surrounding talking about [suicide] that we have got to break through." This target, at least, is now one step closer: the senate unanimously passed the bill in December 2012, and it has become law. The federal government has 180 days to appoint an agency to lead a consultation with stakeholders about the next steps in acting on the legislation.

To date, there has been no official announcement about who will take responsibility for the consultations, though several national bodies such as the Public Health Agency and the Mental Health Commission are well positioned to assume such a mandate. Until a more defined course for a national suicide prevention strategy is set, the bill's impact will remain uncertain. For now at least, Harold Albrecht, CASP, and families across the country may find hope in knowing that a small, but important step has been taken towards preventing suicide. ■

Acknowledgements

The author would like to thank Harold Albrecht and Dr. Paul Links for taking part in interviews for this report.

For More Information

Canadian Association for Suicide Prevention
www.suicideprevention.ca

Mental Health Commission of Canada
www.mentalhealthcommission.ca

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Nathaniel Pollock

Nathaniel is a 3rd year PhD student from the Division of Community Health and Humanities in Memorial University's Faculty of Medicine. His research examines the role of mental health services in preventing suicide in northern and aboriginal communities. His project is being conducted at MUN's Labrador Institute in partnership with the health authority and Aboriginal governments in Labrador. Nathaniel lives with his family in Happy Valley-Goose Bay.

News Article

We are what we eat: Can our diet shape communication between gut microorganisms and the brain to determine disease development?

Jennifer Beatty *(University of Calgary)*
News Reporter (HSI 2012-2013)

Autism Spectrum Disorder (ASD) encompasses autism, pervasive developmental disorder not otherwise specified (PDD-NOS), and Asperger's disorder. These neurodevelopmental conditions present clinically as impairments in social interaction and communicative abilities, as well as through strong tendencies towards repetitive interests and behaviors.[1] Using a sample of 11 children, Leo Kanner was the first to document observations of severe communication problems, abnormal social interactions, and stereotypical behaviours, such as repetitive rocking.[2] Kanner's initial description of this "syndrome" set the framework for the subsequent compartmentalization of afflicted children into the realm of ASD.

The incidence of ASD has increased significantly in the past two decades; in 1992, 19 in every 10,000 American children were estimated to suffer from ASD,[3] with that number increasing to 90 cases in 10,000 as of 2006.[4] Population-based studies of ASD prevalence in Canada are limited; however, one study suggested 65 per 10,000 children to be afflicted.[5] It is becoming evident that there are increasing rates of ASD and other neurodegenerative disorders in countries around the world that have adopted westernized eating and lifestyle habits, including increased consumption of processed carbohydrates.

"There are a lot of changes happening in human health over the recent years, and the effects of such are staring us in the face."
Dr. Derrick MacFabe

Enhanced diagnostic procedures, as well as increasing societal awareness of ASD and associated disorders, may contribute to enhanced detection in this country, but many experts agree that other factors must be at play. Dr. Derrick MacFabe, a leading researcher at the University of Western Ontario (UWO), agrees, saying:

There are increasing rates of ASD and other neurodegenerative disorders in countries around the world that have adopted westernized eating and lifestyle habits, including increased consumption of processed carbohydrates. *(Flickr: cindy1379)*

"There are a lot of changes happening in human health over the recent years, and the effects of such are staring us in the face." Indeed, the changes alluded to can include the overconsumption of carbohydrates, misuse of antibiotics, and exposure to such things as environmental pollution, heavy metals, and herbicides. Dr. MacFabe himself has spearheaded research initiatives aimed at characterizing a link between Canadian nutrition habits and the effects on the resident gastrointestinal (GI) microbiota, as well as the resulting impact on the development of ASD.[7] He credits pioneers in the field, such as Dr. Sidney Finegold, for establishing connections between perturbed microbial populations in the guts of children with regressive forms of ASD.

Dr. MacFabe readily agrees that the examination of a link between bacteria in the gut and pertinent effects within the central nervous system may seem far-fetched – at least upon first thought. However, he became increasingly interested in following documentation in the literature recognizing abnormal populations of certain bacterial groups, including clostridia and desulfovibrio, in stool samples of patients with autism. It was here that he began to question the possible outcomes that such changes in the gut may have in the brain. It was on this quest that Dr. MacFabe recognized the importance of defining metabolic markers, particularly from gut microbial populations characteristic of children with ASD, that can be isolated and tested for effects in animal models of disease. ▶

MacFabe defines particular short-chain fatty acids (SCFAs) as natural forms of metabolites that are produced by members of the gut bacterial microbiota upon ingestion of carbohydrates.[7] He particularly focuses on propionic acid (PPA), as it is an intermediate SCFA that is a normal part of carbohydrate metabolism.[7] Dr. MacFabe points out "…that there is a higher concentration of PPA in stool samples from children with autism than in their healthy counterparts." Consequently, for his research group the question quickly became whether PPA provided a link between dietary carbohydrate intake, altered microbiota, and effects within the central nervous system capable of producing ASD-associated symptomology.

"A good model of disease is one which can link findings from multiple models," says Dr. MacFabe, who also emphasizes the initial importance of determining a central effect of PPA in the brain. Indeed, Dr. MacFabe says, "We were shocked to see in adult animals with intact nervous systems [that] small amounts of PPA administered into the brain proved to have a central effect by eliciting significant hyperactive, repetitive, and ignoring behaviors," typical of observations from many behavioral models of ASD. This work is groundbreaking in its demonstration that a broad level, common metabolite of gut bacteria can elicit significant behavioral effects.

Subsequent studies performed by MacFabe and his team have shown additional changes in the immune profile of animals administered PPA; these changes are seen in both innate and neuro-inflammatory markers. The study, released by the Journal of Translational Psychiatry in January 2013, identified a large sub-group of ASD patients exhibiting biomarkers for abnormal fatty-acid metabolism.[6] These findings have begun to bring much of the work done in the PPA-administered rat model full-circle, as they suggest an important overlap between a promising animal model and a real life disease situation.

The work done by Dr. MacFabe and his team has illustrated the complexity of the human body's interactions with the materials that are ingested from the outside environment, as well as the potential detriments of the carbohydrate overconsumption that is prevalent in our society. The observations have also raised questions about antibiotic administration in the early years of childhood. Dr. MacFabe, however, is quick to shoot down common misconceptions in the media that his research suggests we stop using antibiotics: "These drugs save lives, and I do not condone the ablation of their use." Instead, he suggests looking at the bigger picture and using his observations as a template to help with asking the questions about the mechanisms behind disease development, which requires cross talk in the medical and research communities. Additional misconceptions propagated by the media can also cloud the reality of scientific progress; the result is desperate parents looking for quick cures to their child's ASD. "Many desperate parents may not appreciate what is needed ethically before treatments are accessible," says Dr. MacFabe. This further highlights the need for additional research in the areas surrounding the impact of our environment on the human body; it also highlights the need to exploit novel model systems – animal *and* in vitro – to help give us a glimpse behind important initiation events leading to neurological conditions such as ASD. ■

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Jennifer Beatty

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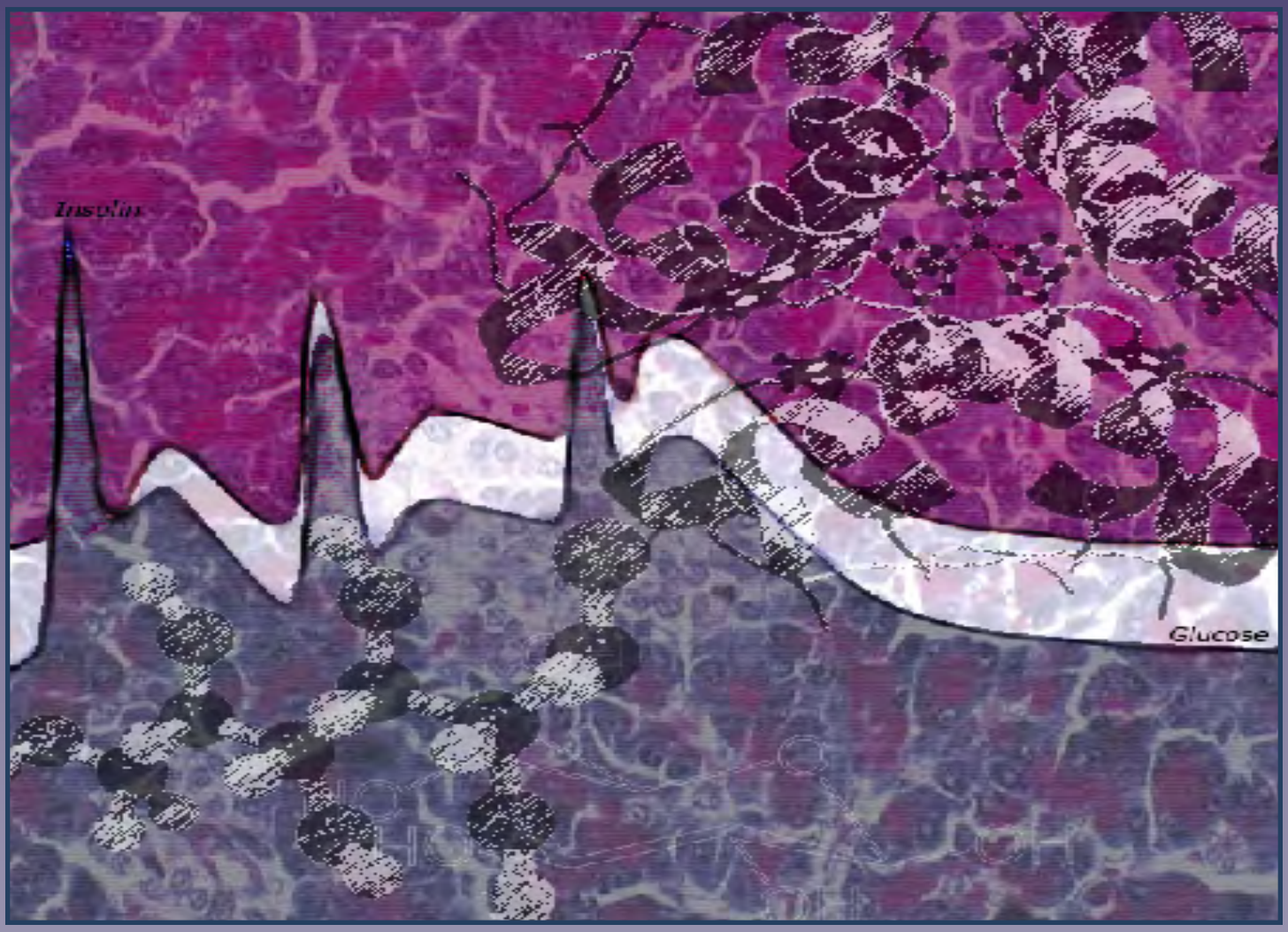

SECTION 2: DIALOGUE PIECE

HSI invited an expert in the field of Mental Health and Neurological Disorders research to write a 1000-word essay on a controversial topic that would generate discussion amongst our staff members and general readership. This year, Benoit Labonté engages readers with a detailed piece how epigenetic changes can modify our behaviours early on in life.

HSI Editorial Team members were then asked to submit comments in response to this stimulating piece of writing. These responses were aimed at questioning and challenging the original author's viewpoints in a respectful manner. The original author was then asked to submit a 500-word response to the comments written by the HSI Editorial Team.

In our second dialogue piece, Diana Clarke - from the American Psychiatric Association - uses her expertise to outline the main changes of the DSM-5. It's an insightful piece that is bound to generate discussion among students and physicians who study and practice psychiatry.

The epigenetic component of early-life adversity

Benoit Labonté

Introduction

The debate on nature versus nurture has already generated lots of discussions. While it has long ago been noted that adverse events occurring early in life increase the risk of developing psychiatric disorders, identifying and characterizing the mechanisms by which these effects are mediated has been challenging. Thus, only recently has evidence allowed researchers to identify potential mechanisms by which the environment may induce behavioral effects. Indeed, epigenetics is now perceived as a potential mechanism by which cells, and by extension complete organisms, may adapt to their environment.

Epigenetics

Epigenetics refers to the study of the epigenome, the chemical structure surrounding DNA and interfering with normal gene expression without altering the DNA sequence itself. Classically, two main mechanisms have been described: DNA methylation[1] and/or hydroxymethylation,[2] and histone modifications.[3] By interfering with the recruitment of the transcriptional machinery to the DNA, hypermethylation in promoters has classically been associated with transcriptional repression[1] although more recently, intragenic methylation and hydroxymethylation has been suggested to promote the expression of alternative transcripts and splicing variants.[4,5] Alternatively, chromatin modifications are known to change chromatin structure (euchromatin/ heterochromatin) and promote or repress access of the transcriptional machinery to the DNA.[3] Importantly, these transcriptional regulatory mechanisms have been shown to be susceptible to environmental challenges such as early-life adversity, having the consequences of interfering with normal gene expression and to be potentially associated with behavioral modifications during adulthood.[6]

The Impact of Early-Life Stress on Gene Expression

By definition, early-life adversity is expected to generate a climate of intense stress that may often be persistent in time. As such, one of the systems that is the most likely requested by early-life adversity is the hypothalamic-pituitary-adrenergic (HPA) axis, which regulates biological and physiological responses to stress. Early groundbreaking work from the lab of Dr. Michael Meaney showed that variation in maternal care induces changes in the expression of the glucocorticoid receptor (GR17) by altering DNA methylation patterns in the GR regulatory region. Following this elegant piece of work, translational studies showed that similar alterations may also take place in the brain of suicide completers with a history of child abuse. Indeed, McGowan and colleagues showed that abused suicide completers had lower GR 1F (GR 17 homologue) expression levels that were associated with higher DNA methylation levels within GR 1F promoter. Together with other studies on the epigenetic regulation of GR by stress,[7,8] these findings suggest that the whole GR locus may be poised to epigenetic regulation by environmental stressors such as early-life adversity.

Besides GR, several other genes have been shown to be susceptible to the effects of environment. For instance, other constituents of the HPA axis such as the arginine vasopressine (Avp)[9] and the corticotrophin releasing hormone (CRH)[10] genes have been shown to be epigenetically disrupted by stress in rodents. Interestingly, these findings correlate with previous human work showing alterations in the expression of CRH and pro-opiomelanocortic (pomc) genes in the brain. Similar animal/human correlations can also be made with findings concerning stress-induced regulation of neurotrophins (brain-derived neurotrophic factors; BDNF, glial-derived neurotrophic factor; GDNF)[11] and their receptors (tyrosine kinase receptor type B; TrkB). Indeed, social stress in mice and rats was shown to interfere with the expression of BDNF in the hippocampus by altering ▶

histone modification and DNA methylation signatures.[12-14] In humans, both BDNF and trkB (T1 subtype) were shown to be epigenetically dysregulated in the brain of depressed suicide completers.[15-17] Several other examples of stress-induced epigenetic alterations in animals and humans have been reviewed elsewhere.[6,18]

Genome wide approaches

These findings clearly support the involvement of epigenetic mechanisms in mediating the impact of the environment on gene expression and behavior. However, it is unlikely that only a subgroup of genes may be targeted by early-life adversity as these effects may rather be found across the genome. We recently addressed this question by doing a genome wide screening of promoter DNA methylation patterns in the hippocampus of severely sexually and/or physically abused and non abused suicide completers.[19,20] Our data showed the presence of hundreds of sites differentially methylated in the promoters of abused and non abused suicides. Importantly, DNA methylation was shown to be inversely correlated with gene expression across the genome.

Note that a proportion of differentially methylated genes was common to the abused and non-abused suicide groups. Although a large proportion were unique to the abused suicides, suggesting that child abuse may impose a certain remodeling of DNA methylation signature in gene promoters. This was confirmed by comparing functions being enriched with differentially methylated genes. Indeed, while cell plasticity was among the most significantly affected functions in the brain of abused suicide completers, functions related to learning and memory processes were unique to the suicide group. Both of these functions are relevant to abuse and suicide, as studies in rodents showed that early life stress decreases adult hippocampal neurogenesis[21,22] and human studies suggest that learning and memory deficits are symptoms frequently associated with suicidal behaviors.[23,24] It is also interesting to mention that similar findings have also been reported in peripheral samples of post-traumatic stress disorder (PTSD)[25] patients and in the prefrontal cortex (PFC) of psychotic and bipolar subjects.[26]

Limitations and future perspectives

Up to date, most studies focused on brain tissue as this strategy holds the promise to helping improve our understanding of the impact early-life adversity has on brain functions. However, it is still unclear whether these findings will be useful for identifying individuals with specific predispositions toward psychiatric disorders. As such, it will be important to run similar studies in easily accessible tissue such as blood or saliva and to define whether the alterations found in the brain can also be found in peripheral tissue and vice versa. Besides the beneficial effects these studies will have on defining the pathological processes triggered by early-life adversity, it will also allow the identification of predisposed individuals to psychiatric disorders and help in defining better treatment strategies.

Working with animal models helps to generate new working hypotheses. It is, nevertheless, important to determine whether findings can be translated in humans. Presently, working with human samples is challenging given the high level of variability that exists between subjects. No one can assume that each individual went through the same life events, had the same life experience or have the same comorbid disorders. In addition, human postmortem brain studies often have to deal with relatively small sample size given that the resources are rare and precious. It is therefore important to appreciate these limitations, many of which can hardly be addressed with means other than statistics, when considering this type of studies.

Finally, it is important to understand that epigenetics has an integrated and dynamic process involving several components. As such, it will be important to interpret findings in a broader context, by integrating findings from several epigenetic markers (i.e. DNA methylation, hydroxymethylation, several histone modifications) and visualizing their evolution over time. With technology evolving, it will be important to perform more large screening studies looking at the relationship between several markers in the same cell population. In addition, it is important to note that findings summarized previously are actually snapshots of epigenetic signatures at the moment of death. One may expect these alterations to be dynamic over the lifespan. Future studies in animals or humans (peripheral samples) may aim to assess the evolution of these markers in relation to the development of psychiatric conditions.

Conclusion

There is a growing body of evidence suggesting that the behavioral effects of early-life adversity may be mediated via epigenetic mechanisms. As such, epigenetics may represent an interface on which the environment acts to induce behavioral effect by altering normal gene ▶

expression. While previous studies convincingly supported this hypothesis, it will be important to launch more large-scale comprehensive studies and take advantage of valid and well defined animal models to test and develop new hypotheses. With that being said, it will be necessary to expand this field of research as it has the potential to significantly improve our understanding of mental health and help to define better intervention strategies. ■

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Benoit Labonté

My research interests are to define the molecular impact of stress in the brain and to determine how these effects can affect behaviors and mental health. To do so, I study epigenetic mechanisms, mainly DNA methylation, chromatin modifications, and small RNAs. With my studies, I try to define how genes are influencing behaviors and how changing the function of a gene, by affecting epigenetic mechanisms can have distinct and profound impact of cell functions what can then be translated to a behavioral effect.

My future objectives are to develop my expertise in this highly interesting and stimulating field of research and then get my own lab in order to expand our understanding of stress and mental health.

Comments on Dialogue Piece #1 (from HSI Members)

Comment 1

This dialogue piece has shed light upon the intricate interplay between genes and the environment, and it has also illustrated one of the mechanisms by which childhood trauma may leave an indelible impression on the human brain.

Providing the vital link between nurture and nature, this exciting piece of research describes how high-throughput techniques can be used to identify epigenetic changes that may arise from abuse events in early childhood.

But this study also raises many interesting questions.

For instance, let us momentarily assume an evolutionary psychology perspective. Through this lens, we can assume that neurological events, like all biological events, are the result of selective pressure. Thus, an epigenetic response to an abuse event might be either (a) an evolutionarily-selected response to abuse or (b) the byproduct of some other evolutionarily-selected response to abuse. It would be very interesting to hear the author's perspective on whether the observed epigenetic responses to abuse confer some form of adaptive benefit – i.e., could the new pattern of gene expression help form a "mental barrier" between the individual and the traumatic events they endured?

At the cellular level, it would be interesting to examine the functional consequences of these epigenetic changes. Are parameters such as neural connectivity, neural distribution, synaptic function, and neurite outgrowth affected by these epigenetic changes? In the absence of patient neuronal samples for such experiments, it is possible that induced pluripotent stem cell-derived neurons, such as those used to model schizophrenia in the laboratory of Dr. Fred Gage at the Salk Institute for Biological Studies,1 could be used to answer these questions.

From a macroscopic perspective, it would also be very interesting to determine whether epigenetic changes occur at the community level – perhaps in response to a collective trauma such as war or natural disaster. Such studies might also elucidate whether there is an age constraint to this effect, after which epigenetic changes in response to stress or trauma may not be as pronounced.

Brie McKenzie (HSI Managing Editor, Spotlight on Careers)

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Comment 2

"A mind that is stretched by a new experience can never go back to its old dimensions."[1] While the late American Supreme Court Justice, Oliver Wendell Holmes Jr., may have been speaking metaphorically, the exciting new field of epigenetics sheds light on how experiences and memories, or nurture, can trigger the modification of the functional expression of genes. These impressions can have long-lasting effects on the brain and behaviour of the individual, altering responses to similar events later in life, as well as potentially impacting future offspring. As such, I agree with the author who champions epigenetic research as a way to "define pathological processes triggered by early-life adversity… identify predisposed individuals to psychiatric disorders and help in defining better treatment strategies" (p. 32, *this issue*). However, the experience of early-life adversity does not necessarily lead to future psychopathology. Thus I propose expanding the knowledge generation potential of epigenetic research to include an understanding of resiliency.

During the critical period of fetal development there is lots of opportunity for epigenetic variation in response to maternal adversity. But how can health professionals council mothers and families to buffer the long-term effects of adverse pregnancy experiences? In 2004, Canadian researchers discovered the nurturing behaviour of rats resulted in the change of an epigenetic mark at a gene that triggered calm responses to startling in offspring.[2] Importantly, this epigenetic modification lasted with the animal throughout its life. While humans and rats are markedly different, this finding could mean that attentive interaction between parent and child could dramatically increase resiliency in children that would carry into adulthood. Certainly this area warrants further investigation. Maternal trauma may be uncontrollable, but providing parents with tangible strategies to give children the best possible chance despite experiencing early-life adversity puts a degree of control back into their hands.

Jennifer Kramer (HSI Reviewer)

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Author Response to Comments on Dialogue Piece #1

The environment has been known to affect behavior, but it has been challenging to illustrate how this actually happens. Following a growing body of evidence, it is now suspected that epigenetics may be one mechanism in which the organism adapts to environmental pressures. This concept, which can be referred to as resilience, allows the organism to maintain a certain level of physical and psychological functional activity. Related to mental health, resilience may be defined by the capacity of an individual to avoid negative social, psychological and biological consequences of extreme stress that would otherwise compromise their psychological or physical well-being.[1] Early-life adversity, and particularly childhood abuse, is a major risk factor for the development of mental disorders[2] but it is important to mention that not all abuse victims develop psychiatric disorders and suicidal behaviors. This suggests that the mechanisms that protect the organism from the threat of abuse may be inefficient in a subgroup of individuals which may then develop mental disorders and potentially suicidal behaviors in the most extreme cases.

Interestingly, certain animal models of stress-induced depression also show a certain animals are non-susceptible to stress. For instance, in one study about 65% of social defeated mice will show depressive-like behaviors while 35% won't behave differently from controls; the phenomenon has been interpreted as resilience.[3] Moreover, these resilient animals don't show the epigenetic alterations found in the susceptible group following stress, but, rather, look like the controls.[1] These findings suggest that there are epigenetic mechanisms which may be involved in establishing a barrier to the detrimental molecular impact of stress in the brain, and, consequently, protecting the animal from depressive-like behaviors.

Importantly, the detrimental effects of early-life stress seem to be potentially reversed if specific measures are taken into a critical time window. For instance in rats, Michael Meaney and colleagues showed that the pups raised by mothers providing poor maternal care (i.e., low licking and grooming; low LG) behave similarly to pups raised by normal mothers if these pups are cross-fostered to mothers exhibiting high maternal care (high LG) during the first week of life.[4] Importantly, these measures also reverse the hypermethylation in GR17 promoter found in the low LG group, suggesting that these effects can be reversed if drastic measures are taken before a critical time frame.

Studying resilience in human has been more challenging. For instance, a growing body of evidence suggest that certain personality traits and involvement in religion and community are associated with resilience.[5] Interesting finding from the group of Dr. Monique Seguin showed that, similar to the findings in rats, life trajectory can be modified if specific measures are taken in early-life (unpublished data). For instance, children with a history of abuse or maltreatment are known to develop life trajectories with poor outcomes, and are more likely to experience mental health problems. However, changing the dysfunctional family environment has been shown in some cases to improve life trajectories. The mediators and moderators involved in these effects are still unknown, but evidence for epigenetics is starting to accumulate. For instance, abuse victims show DNA methylation changes that are not found in the non-abused group. While these changes are associated with changes in gene expression, one may hypothesise that they represent an attempt to modify gene expression patterns in order to adapt to the environmental treats. However, the consequences of these changes appear to be detrimental.

One may hypothesize that these changes may initially have been advantageous for dealing with the occurrence of severe stressors like repeated abuse. However, they may have lost their positive impact as the abuse victims became adults. Indeed, these changes appear to be stable overtime and what was initially advantageous at the moment of the abuse may become disadvantageous in adults. This may be especially true given that these adverse events happen during childhood and adolescence in a period of high plasticity for the developing brain. The long lasting genome-wide changes in DNA methylation may interfere with the establishment of appropriate behavioral and emotional schemes. Consequently, abuse victims are more likely to exhibit stress responses associated with maladaptive emotional and behavioral responses to daily life stressors, which is believed to increase the risk for depression and suicide.[6]

Up to date, it has been challenging to test these hypotheses in the lab and obtain molecular answers using classic methods. However, the development of new approaches may help in obtaining more precise answers. One of these methods involves the use of induced pluripotent stem cells to model depression in a Petri dish . This method consists in taking pluripotent stem cells from a patient with a specific psychiatric illnesses, and treating their cells ▶

Author Response to Comments on Dialogue Piece #1

with various transcription factors in order to make them differentiate into specific cell types, including neuronal progenitors. These techniques have proven to be informative on the cellular alterations that may be taking place in certain psychiatric conditions, including scizophrenia.[7] It will be interesting to see whether these methods can also be used to study depression and possibly even the molecular and cellular impact of early life stress. However, before getting these answers, it will be important to determine whether inducing by artificial means neuronal differentiation also impacts the epigenome (DNA methylation and chromatin marks), which is known to be highly involved in defining cellular fate across development. But, if this appears to be a minor issue, iPSCs may represent a very powerful model to study the cellular and molecular impact of chronic stress on neurons.

Studying the molecular impact of stress in the brain has highlighted a whole new field of research that may help to clarify certain aspect of stress and psychiatry. Consequently, researchers are starting to study the molecular and epigenetic components potentially involved in post-traumatic stress disorders (PTSD) at a larger scale. For instance, researchers are now studying the impact of civil war in larger community and in war veterans . Others are investigating the long term effects of chronic food deprivation following episodes of famine in certain regions of the world . It will be interesting to follow-up on this work in the coming years, and to continue using animal models, to have deeper insights into the molecular mechanisms regulating the impact of stress on behavior and mental health. ■

Benoit Labonté

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Finalization of DSM-5, Part I: Classification and criteria

Diana E. Clarke, Emily A. Kuhl, and William E. Narrow

The Diagnostic and Statistical Manual of Mental Disorders (DSM) is the standard diagnostic system for mental disorders in the United States and numerous healthcare entities around the world, including Canada. The DSM is primarily a tool that was developed to guide to clinical practice through the provision of diagnostic criteria for mental disorders that enabled a common language for clinical communication.[1] In addition to criteria provided to help clinicians determine diagnosis, entries are accompanied by diagnostic codes – largely used for billing and administrative purposes – and narrative text that expounds on features relevant to assessment and research, such as age, gender, and cultural-related information; development and course of illness; prevalence; and differential diagnosis. In addition to its central role as a tool for patient care, the DSM is used by researchers, insurance companies, legislators and policy makers, and health statisticians. Revisions are coordinated by the American Psychiatric Association (APA) and have generally been undertaken every 15-20 years.

The Fifth Edition of the DSM, DSM-5, was published in May 2013, following a decade-long development process to review the scientific foundations and clinical utility of the manual and, when indicated, develop new criteria and text. This revision was driven by evidence from the clinical, epidemiological, neuroscience, and genetic literature, which suggested that the criteria and categorical classification approach used in the DSM-IV no longer reflected the evidence or patient and clinician realities, and had started to hinder research progress. The literature also identified serious implications associated with the use of the DSM-IV, including the over-occurrence of multiple diagnoses within the same patients, excessive use of "not otherwise specified" diagnoses, and an over-emphasis in research on criteria reliability rather than other important indicators, such as clinical utility, feasibility, and validity. These issues formed the basis of the DSM-5 Task Force and Work Groups proposals to develop the DSM-5. The highest priority in the revision of the DSM was to optimize its clinical usefulness with changes guided by clinical and research evidence to bring better scientific and clinical rigor to the diagnosis of mental disorders.

The degree to which the DSM-5 reflects the latest empirical evidence is among the most prominent changes, and is especially recognizable in its revised chapter organization. Previously, diagnostic groups were based on similarities in symptom presentation. But, as our understanding of neuroscience has further developed, it has become clear that classification based on shared genetic and pathophysiological factors, in addition to clinical similarities, will better facilitate research to identify causes of mental disorders, biomarkers, and improved treatments. For example, the most commonly studied mental disorders, autism, attention-deficit/hyperactivity disorder (ADHD), schizophrenia, major depressive disorder, and bipolar disorder, all appear to have significant genetic overlap with one another – a relationship that is particularly strong for schizophrenia and bipolar disorder.[2,3] Accordingly, the DSM-5 places the chapters on neurodevelopmental disorders (which include autism spectrum disorder and ADHD), schizophrenia spectrum and other psychotic disorders, bipolar and related disorders, and depressive disorders proximal to one another.

Advances in pathophysiology, brain imaging, and neurogenetics also informed the need to redistribute certain disorders from their DSM-IV classification. For instance, the DSM-IV's anxiety disorders now exist across four different chapters in the DSM-5 (anxiety disorders; obsessive-compulsive and related disorders; trauma- and stress-related disorders; and dissociative disorders). Recent studies have shown that obsessive-compulsive and related disorders (e.g., hoarding disorder, skin picking disorder, hair pulling disorder, etc.) are likely to involve distinctive neurocircuitry dysfunctions as compared ▶

to other anxiety disorders (e.g., social anxiety disorder [social phobia], panic disorder, specific phobia, etc.), which supported their disaggregation and redistribution into separate chapters.

The DSM-IV chapter on disorders typically diagnosed in infancy, childhood, and adolescence has been redistributed across different chapters in the DSM-5 based upon scientific evidence of their biologic relatedness. For instance, separation anxiety disorder and selective mutism are now in the anxiety disorders chapter; reactive attachment disorder and disinhibited social engagement disorder in the trauma and stress-related disorders chapter; pica and rumination in the feeding and eating disorders chapter; encopresis and enuresis in a separate elimination disorders chapter; and conduct disorder and oppositional-defiant disorder in the disruptive, impulse-control, and conduct disorders chapters. The DSM-IV's chapter on impulse-control disorders not elsewhere classified is also now more appropriately rearranged across obsessive-compulsive and related disorders (i.e., trichotillomania [hair-pulling disorder]); substance-related and addictive disorders (i.e., gambling disorder); and disruptive, impulse- control, and conduct disorders (i.e., intermittent explosive disorder, pyromania, and kleptomania).

Lastly, the DSM-5's chapters loosely reflect a developmental grouping with conditions more likely to be diagnosed in infancy and childhood placed earlier in the manual (e.g., neurodevelopmental disorders), conditions diagnosed in later life placed near the end (e.g., neurocognitive disorders), and those commonly seen in adulthood generally in the midsection of the manual. This is also replicated in the listing of disorders themselves within several, though not all, of the chapters, including the chapters on depressive disorders (i.e., disruptive mood dysregulation disorder [DMDD] listed first), anxiety disorders (i.e., separation anxiety disorder and selective mutism are the first two listed), trauma- and stress-related disorders (i.e., reactive attachment disorder and disinhibited social engagement disorders are the first two listed), and feeding and eating disorders (i.e., pica, rumination, and avoidant/restrictive food intake disorder are the first three listed).

The structure of diagnostic criteria in the DSM-IV is such that individuals either do or do not meet criteria for a disorder, which suggests that there is a discrete boundary between "normal" and "disordered" brain functioning. This is in opposition to much of general medicine: there is no single blood pressure reading, for instance, that demarcates having or not having hypertension ; instead, there are gradients of elevations, from mild, to moderate, and so on, and these delineations are important for informing physicians' treatment decisions. The same is true for the assessment of body mass index, serum cholesterol, glycosylated hemoglobin, left ventricular ejection fraction, etc. In the diagnosis and treatment of mental disorders, little guidance is given for how to account for variations that deviate from the strict criteria and diagnostic thresholds, such as mild symptoms, atypical presentations, or subthreshold symptoms from other disorders. As a result, these patients often land in the "not otherwise specified" (NOS) category of diagnosis, which is not clinically useful and does little to enhance treatment development. This indicates the need for a more dimensional approach to the diagnosis of mental disorders or, at least, the need for a combined categorical-dimensional system.

The move towards a dimensional approach is slow but ongoing. In the DSM-5, efforts were made to include different levels of dimensional assessments that can be employed to better characterize distinctions of disorders. These include, for instance, clinician and patient (or parent/informant) rated dimensional assessment of symptom domains that are important across all mental disorders (i.e., cross- cutting measures), and patient (or parent/informant) assessment of disability. Included in the main sections of the manual (i.e., Section II) are clinician-rated dimensional assessment of the severity of some, but not all, DSM-5 diagnoses, such as autism spectrum disorder, substance use disorders, anorexia nervosa, and bulimia nervosa. The patient (or parent/informant) rated cross-cutting, diagnostic-specific severity, and disability measures are included in Section III of the manual and in the online supplemental materials for the DSM-5 (http://www.psychiatry.org/dsm5). Section III indicates the need for further testing in the field. Clinicians and researchers are encouraged to evaluate the measures' usefulness in describing patients' clinical status and response to treatment.

The cross-cutting dimensional measures assess symptoms that cut across most, if not all, mental disorders – such as depressed mood, anxiety, cognition problems, substance use, and sleep disturbance – is analogous to general medicine's review of systems. This measure calls attention to symptoms that may or may not indicate the presence of a disorder (but nonetheless may indicate a need for treatment), and could otherwise be overlooked during clinical exam. If endorsed, a second level of dimensional assessments can be administered to explore the symptom(s) in greater detail, providing clinicians with clues as to ▶

whether related symptoms or, possibly, even a full disorder may be present. If a clinician determines that a disorder is present (based on responses to dimensional assessments as well as diagnostic interview and clinical judgment), another level of dimensional assessment can provide quantitative ratings of the severity of the disorder, which help establish baseline functioning and aid in tracking clinical course and treatment response. Finally, inclusion of the World Health Organization Disability Assessment Schedule (WHODAS) 2.0 provides an alternate method for the assessment of disability and functioning. The WHODAS 2.0 allows for a thorough assessment of disability and functioning without confounding from the effects of symptoms. The fact that these dimensional measures are completed by the patient (or parent/informant) is reflective of recent healthcare trends to more actively adopt patient-reported outcomes as part of clinical care, which may improve decision-making and quality of care and is already standard in clinical trials and drug and device labeling.

Beyond the organization of the diagnostic chapters and disorders, other notable modifications were endorsed to improve clinical care, such as the addition of new disorders. Autism spectrum disorder (ASD), which folds DSM-IV's autism, Asperger's disorder, childhood disintegrative disorder, and pervasive developmental disorder NOS, was proposed after a rigorous review of existing data indicated the disorders were not consistently and reliably diagnosed and that evidence indicating their unique associated features, familial history, treatment response, and prognosis was lacking.[4] However, the DSM-5's specification of the severity of social communication impairments and restricted repetitive patterns of behaviours, variability, onset, and course led to inclusion of ASD specifiers to demarcate particular presentations, such as whether or not accompanying intellectual impairment or language impairment are present. This will allow children to be diagnosed more accurately while preserving the DSM-IV disorders that allow already-diagnosed individuals to receive insurance coverage and educational assistance.

Major neurocognitive disorders (NCD) replace DSM-IV's various dementia and amnestic disorder diagnoses. Mild neurocognitive disorders were approved as mental disorders for the DSM-5, after having been in the appendix of the DSM-IV. Each is accompanied by specific subtypes, including diagnostic criteria and text, to help better describe potential underlying causes of the cognitive impairment, including Alzheimer's disease, HIV infection, vascular disease, traumatic brain injury, and frontotemporal disease. Individuals with these disorders are frequently the subject of research and treatment development, and the provision of specific criteria and more detailed text descriptions for each of the NCD subtypes should facilitate advances in those areas. These patients are also often encountered in clinical settings, and the revised criteria should yield more accurate and reliable diagnoses.

Among other new disorders are hoarding disorder, premenstrual dysphoric disorder, DMDD, binge eating disorder, restless legs syndrome, REM sleep behaviour disorder, and excoriation (skin- picking) disorder. Proposals for novel diagnoses were developed only after the DSM-5 Work Groups conducted thorough literature reviews and, in some instances, secondary data analyses to determine the validity and public health need for inclusion. Some proposals did not meet the standard for inclusion set by the various review committees charged with assessing all major proposed changes to the DSM-5, and in many cases, those proposals were accepted into the DSM-5's chapter on Conditions for Further Study. These include attenuated psychosis syndrome, caffeine use disorder, Internet gaming disorder, and non-suicidal self-injury. While criteria and text are provided for each of these, they are not considered official mental disorders and their criteria are not to be used clinically; they are primarily for further research to determine whether inclusion in a future edition of DSM is warranted.

In summary, the development of diagnostic criteria that are completely dimensional and/or are based entirely on biological and genetic markers would be ideal since this would provide for more reliable and valid diagnosis of mental disorders. However, in the absence of such biological and genetic markers, and with a focus to enhance the diagnosis and care of patients with mental health problems, the DSM-5 has relied on clinical experience as well as existing and growing empirical evidence to guide the revision process. This has resulted in an updated manual that will help clinicians better describe and diagnose their patients. The inclusion of clinicians' dimensional rating of the severity for some diagnoses is a significant step towards this endeavor to have a more dimensional assessment of mental disorders. The DSM-5's cross-cutting dimensional measures are also a major step towards this endeavor. This is complementary to the National Institute of Mental Health's Research Domain Criteria (RDoC) initiative, which calls for the development of "new ways of classifying psychopathology based on dimensions of observable behaviours and neurobiological measures."[5] While the RDoC emphasises the dimensional approach to the classification ▶

of psychopathology from a more basic science perspective, the DSM examines similar issues from a clinical research and practice perspective. It is hoped that, with continuing research, the two approaches will merge, resulting in a clinically useful diagnostic system that is fully informed by neuroscience and basic behavioural science. ■

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Diana E. Clarke

Dr. Clarke is the Research Statistician/Epidemiologist with the American Psychiatric Association Division of Research and the American Psychiatric Institute for Research and Education, and the an Adjunct Assistant Professor in the Department of Mental Health at Johns Hopkins Bloomberg School of Public Health. Her work with the APA over the past 4 years has centered on conducting research studies using data from a variety of sources to help inform the DSM-5 revision process. This includes the planning, development, implementation, and overseeing the multisite DSM-5 field trials and working as a member of the DSM-5 Research Group and the DSM-5 Study Groups on Gender and Cross-Cultural Issues, Impairment and Disability, and Diagnostic Assessment Instruments. Her research interests are centers on the epidemiology of mental disorders and specifically on obtaining accurate assessments of mental health predictors and outcomes such as apathy, dementia, depression, and suicidal behaviors. She received a bachelor's degree with majors in biology and psychology from York University, her master's and doctorate degrees in Epidemiology and Aging from University of Toronto (CIHR-funded), and postdoctoral fellowships in Psychiatric Epidemiology in the Department of Mental Health at Johns Hopkins Bloomberg School of Public Health funded by the Canadian Institute for Health Research, in Psychiatric Epidemiology and Population Health Studies funded by the Department of Psychiatry, University of Toronto, and in traumatic brain injury research at Toronto Rehabilitation Institute and University of Montreal. She has received a number of awards for her research and studies in Aging and the Life Course as well as her research on suicidal behaviors in Holocaust survivors and traumatic brain injury. She has participated in several collaborative research projects at CAMH, Toronto Rehabilitation Institute and the APA, including the DSM-5 Field Trials.

Emily A. Kuhl

Emily A. Kuhl, Ph.D., is the Senior Science Writer and APA/DSM-5 Text Editor at the American Psychiatric Association. Her primary involvement in DSM-5 was in editing and coordinating the production of the draft manual and in serving as the principle writer and editor for scientific and lay audience publications related to DSM-5. Dr. Kuhl completed her doctoral degree in clinical psychology from the University of Florida with a specialization in behavioral cardiology. Prior to graduate school, she was a copyeditor and writer at a daily newspaper in suburban Washington, D.C. She is a member of the American Medical Writers Association and the National Association of Science Writers.

Dr. William Narrow

Dr. William Narrow is the associate director of the American Psychiatric Association Division of Research and the American Psychiatric Institute for Research and Education, and the Research Director for the DSM-5 Task Force. His research interests are centered on the epidemiology of mental disorders and mental health services research, in particular disability related to mental disorders and the estimation of need for care. He received a bachelor's degree (summa cum laude) with majors in biology and sociology from Boston University, a medical degree from Temple University, and a master's degree in public health from the Johns Hopkins University. Dr. Narrow completed an internship in internal medicine at Michael Reese Hospital, specialty training in psychiatry at the University of Chicago, and a fellowship in epidemiology at the National Institute of Mental Health. Before his appointment at the APA in 2001, Dr. Narrow was senior advisor for epidemiology in the Office of the Director at the National Institute of Mental Health (NIMH). He has participated in several collaborative research projects at the APA and NIMH, including the DSM-5 Field Trials, an NIH-funded conference grant to develop a DSM-V research agenda, for which he was co-principal investigator, and the editorial board for development of the Diagnostic Interview Schedule for Children (DISC-IV). He is also an editor of the journal Social Psychiatry and Psychiatric Epidemiology.

SECTION 3: MAIN SUBMISSIONS

Call for Submissions

Back in October 2012, graduate students from all across Canada were asked to submit commentaries on various aspects of Mental Health and Neurological Disorders. The commentaries were 700-800 words in length (maximum of 10 references) and focused on one of three specified topics of interest:

- Social, Economic, and Environmental Determinants of Mental Health and Addiction
- The Aging Mind: Alzheimer's, Parkinson's, and other Age-Related Neurodegenerative Disorders
- Advances, Challenges, and Controversies in the Diagnosis, Treatment, and Management of Mental Health and Neurological Disorders

Review / Revisions

Starting in March 2013, each submission was reviewed by 2-3 different Reviewers from HSI. Reviewers provided feedback to the authors by critically assessing the content and writing of each commentary. After receiving comments from Reviewers, authors were given 2 weeks to revise their submission and resubmit their manuscript to the journal. A team of Senior Editors was then given the task of going through each commentary and providing final comments.

Judging Process

Faculty members from Canadian universities (see Page 45) were recruited as advisors, playing an instrumental role in the judging process of the journal. For each of the above three categories, 4 faculty advisors were assigned to rank each of the submissions in order of preference. A score was then assigned to each paper depending on how it was collectively ranked by all faculty members:

Example: Rank #1: Paper 1C = 5 Points
Rank #2: Paper 1A = 4 Points
Rank #3: Paper 1D = 3 Points

Section 3: Main Submissions

Winners

After processing the rankings from all our faculty advisors, a combined score was tabulated for each submission. The authors of the highest scoring paper for each category received a free 1-year subscription to Annals of Internal Medicine. In addition, one of the papers was granted expedited review for possible publication in Annals of Internal Medicine, Journal of Mental Health, and Canadian Journal of Community Mental Health.

The quality and creativeness of all the submissions were outstanding, and both the editorial team and faculty advisors highly commend the authors for their achievement and hard work! After tabulating the results, we are pleased to announce the winning submissions for the 2013 issue of Health Science Inquiry. Each of the authors have received a free 1-year subscription to to either Annals of Internal Medicine, the Journal of Mental Health, or the Canadian Journal of Community Mental Health, and one submission will be granted expedited review and possibly publication in a subsequent issue of the journal.

2013 Winners

Social, Economic, and Environmental Determinants of Mental Health and Addiction

Leigh Vanderloo and Gillian Mandich

Battling bullying: Do obese children face the same fight? *(Page 70)*

The Aging Mind: Alzheimer's, Parkinson's, and other Age-Related Neurodegenerative Disorders

Eli York

A young perspective on an aging disease *(Page 81)*

Advances, Challenges, and Controversies in the Diagnosis, Treatment, and Management of Mental Health and Neurological Disorders

Gregory S. Day and Harry E. Peery

Autoimmune synaptic protein encephalopathy syndromes and the interplay between mental health, neurology and immunology *(Page 89)*

Past Winners

Chelsea Himsworth's paper was published as a 'Reflection and Reaction' piece in a 2010 issue of **The Lancet**: **http://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2810%2970148-1/fulltext**

Timothy W. Buckland's paper was published as a 'Salon' piece in a 2011 issue of **The Canadian Medical Association Journal**: **http://www.cmaj.ca/content/early/2011/10/11/cmaj.111419.long**

Marc Bomhof, Jane Polsky, and Denise Darmawikarta's papers were were showcased on the 'News' section in2012 of the **International Journal of Obesity** website: **http://www.nature.com/ijo/index.html**

JUDGING PANEL

We are very fortunate to have the involvement of 14 distinguished faculty members from all across Canada for this issue of Health Science Inquiry. Each faculty advisor was assigned to one of the three categories students were asked to write commentaries on, and their main responsibilities were to judge and comment on the submissions within each category.

Dr. Robert Brownstone

Departments of Surgery and Anatomy & Neurobiology
Director of Research, Division of Neurosurgery
Assistant Dean
Research - Clinical Departments
Faculty of Medicine
Dalhousie University

Dr. Rob Brownstone, Canada Research Chair in Spinal Cord Circuits, aims to improve the quality of life of people with neurological disorders that affect movement by restoring their abilities to function. He treats patients with Parkinson's disease, tremor and other movement disorders, and is studying nerve circuits that control movement. He seeks to unravel the mysteries of electrical circuits that initiate and control movement.

Dr. Brownstone is studying three crucial circuits: circuits that send messages from the brain to the spinal cord, circuits within the spinal cord that process these messages to coordinate movement, and circuits between the spinal cord and muscles. He is learning how these circuits function in healthy mammals and what happens to the circuits when they are damaged. He has already identified previously unknown nerve populations in the spinal cord and has discovered spinal cord circuits that control the hand's ability to grasp.

The knowledge that Dr. Brownstone is uncovering in his research could lead to the development of strategies that will improve circuit function in people with diseases or injuries affecting movement.

Dr. Rudolf Uher

Associate Professor, Dalhousie University
Canada Research Chair in Early Intervention
Member of the Brain Repair Centre
Staff Psychiatrist, CDHA

Dr. Rudolf Uher, Canada Research Chair in Early Intervention in Psychiatry, believes the reason there is no cure for these illnesses may be due to the fact that treatment starts too late.

Dr. Uher has been exploring the genetic and environmental causes of mental illness to find out if they can help to predict which treatment will work for whom. He is now turning his focus to the early stages of the development of mental illness to see if there are ways to effectively nip it in the bud. His primary interests are early interventions to prevent severe mental illness, classification of psychopathology, the treatment of depression, the use of clinical assessment and genomics to personalize and optimize treatment and the interplay of genes and environment in the causation of mental illness

Dr. Uher is planning to develop targeted interventions in adolescence or early adulthood. He will first test these interventions in young people who are at high risk because one or both of their parents suffer from severe mental illness. If his interventions are successful, they could help many more people lead fulfilled lives without the prospect of mental illness.

Section 3: Main Submissions

JUDGING PANEL

Dr. Philip Ainslie

Associate Professor, Faculty of Health and Social Development, University of British Columbia

Dr. Phil Ainslie, a Canada Research Chair in Cerebrovascular Physiology in Health and Disease, is using sophisticated imaging techniques and other approaches to provide insight into brain function during aging and in selected diseases.

Dr. Ainslie is also assessing how exercise programs can offset declines in brain function. Regular aerobic exercise is already associated with a reduced future risk of heart disease and there is an urgent need for cost-effective interventions that can slow down or prevent normal brain aging and cognitive decline such as dementia.

He believes that by promoting healthy heart function, exercise can diminish disease burden in the brain. The specific focus of his research is directed to the integrated mechanisms which regulate human cerebral blood flow in health and disease. Three main inter-related areas of research are currently being explored: 1) Mechanisms of cerebral blood flow regulation, 2) Influence of environmental stress on cerebrovascular function (with focus on hypoxia and temperature regulation), and 3) Influence of exercise training on cerebrovascular function.

Dr. Ainslie's work will go a long way toward answering why the brain needs the heart to exercise.

Dr. Lisa Kalynchuk

Department of Psychology, College of Arts and Science, University of Saskatchewan

Dr. Lisa Kalynchuk is a Professor and Canada Research Chair in Behavioural Neuroscience. She is utilizing her training in both psychology and neuroscience to tackle affective disorders from two directions – determining the triggers and symptoms of anxiety and depression in adults, and examining how the brain controls the development of the disorders. Working with animal models, Dr. Kalynchuk's research is leading the way toward new and more effective treatments in the future. Her specialties include: Hippocampal function; animal models of depression; behavioural and neuroendocrine correlates of stress; functional consequences of adult hippocampal neurogenesis.

Dr. Robin E.A. Green

Neuropsychologist and Senior Scientist, Toronto Rehabilitation Centre, University Health Network
Associate Professor, University of Toronto
Canada Research Chair (II) in Traumatic Brain Injury

Dr. Robin Green's research focuses on examining the natural history of cognitive and motor recovery following moderate and severe TBI, and in particular why cognitive recovery terminates before its completion. Dr. Green is working on approaches to improve recovery, including increasing therapy hours at different recovery stages; targeted early therapies for brain areas at risk of subacute atrophy; and customized therapy based on individual risk factors.

Section 3: Main Submissions

JUDGING PANEL

Dr. Jodie Burton

Department of Clinical Neurosciences, University of Alberta

Dr. Burton's research activities focus on the clinical aspects of multiple sclerosis (MS). Her main focus of research is on the role of vitamin D in the treatment and prevention of MS, and determination of the appropriate level and dose to achieve meaningful benefits in this population. A safety phase I/II trial of high-dose oral vitamin D3 has been completed. Further research is planned to more rigorously determine the potential role of vitamin D in relapse prevention, MRI activity in those with relapsing MS and its role as a predictor and target in those with a clinically isolated syndrome (the first demyelinating event).

Another area of interest for Dr. Burton is working towards a standardized and validated definition of treatment failure and the risks and benefits of the various management options for those with aggressive and rapidly disabling MS including conventional chemotherapeutic agents and novel immunomodulators. She is also interested in the impact of pregnancy and reproductive hormones on MS activity.

Lastly, she has an overall interest in clinical epidemiology and the design, methodology, and analysis of observational and clinical trials in MS and neurology in general, including demyelinating disease, gender and reproductive hormones in demyelinating disease, optic neuritis and the anterior visual pathway, escalation therapy and stem cell transplantation in demyelinating disease, and neuromyelitis optica.

Dr. Satyabrata Kar

Centre for Prions and Protein Folding, University of Alberta

Dr. Satyabrata Kar has spent the last six years building an independent program for research into Alzheimer's disease. Through his outstanding research and noteworthy record of publications, he has gained the high respect of his peers and students as both a leading neuroscientist and an excellent teacher.

As Chair, Dr. Kar is establishing a premier laboratory for collaborative research related to Alzheimer's and related neurodegenerative diseases. He is pursuing two complementary research themes. One is addressing the interactions between a specific peptide, known as beta-amyloid, and acetylcholine-producing neurons to determine their relevance to changes in the brain tissue of AD patients. The second theme seeks to understand the role of Insulin-like growth factors (IGFs) in normal brain functions and their implications in AD pathology.

The objectives of this work are to uncover why specific nerve cells are vulnerable in AD and to determine whether IGFs or other agents can be manipulated to protect these neurons in AD.

Dr. Souraya Sidani

Professor, School of Nursing, Ryerson University

Dr. Souraya Sidani is a Canada Research Chair and Professor at the School of Nursing, Ryerson University. Her areas of expertise are in quantitative research methods, intervention design and evaluation, and measurement. Her research areas of interest focus on evaluating interventions and advanced practice roles, on examining patient preferences for treatments, and on refining research methods and measures for determining the clinical effectiveness of interventions.

Section 3: Main Submissions

JUDGING PANEL

Dr. Adele Diamond

Head, Division of Developmental Cognitive Neuroscience, University of British Columbia

For over 30 years, Dr. Adele Diamond, Canada Research Chair in Developmental Cognitive Neuroscience, has been studying executive functions and the region of the brain (i.e. prefrontal cortex) on which they rely. Her work integrates behavioural, neuroanatomical and molecular genetic approaches to study how executive functions can be modified by the environment, modulated by genetics and neurochemistry, or become derailed in certain disorders, and effective interventions and ways to prevent disorders.

Her current research is changing our understanding of the prefrontal dopamine system and of gender differences in that, and affecting early education practices about the possibility of intervening early to improve executive functions to head off mental health and academic problems. Her work has shown that executive functions can be improved in very young children by regular teachers in normal classrooms without expensive equipment.

Most recently, Dr. Diamond is turning her attention to the possible roles of play, the arts, dance, storytelling and physical activity in improving executive functions and academic and mental-health outcomes. What nourishes the human spirit may also be best for executive functions.

Dr. Kathy Hegaderen

Faculty of Nursing, University of Alberta

In her research, Dr. Hegadoren is developing models that link trauma experience in women to a scientific understanding of the psychosocial and biological processes involved in their recovery or in their development of stress-related disorders. She carries out prospective psychological studies, brain imaging, and stress hormone studies with women who have experienced traumatic events. As well, as a strategy for transferring this knowledge into clinical practice, she develops and tests clinical tools for use in hospital ERs to identify at-risk individuals.

Dr. Hegadoren is also studying the longer-term impact of interpersonal trauma (sexual and physical abuse as a child or adult) on women's health particularly during pregnancy, childbirth, and early mothering experiences. In addition, and in collaboration with other researchers, she is trying to determine the influence a woman's reproductive cycle has on both her stress response and her response to antidepressant therapies. Together, the researchers are assessing the social supports available for women with postpartum depression, characterizing fatigue in major depression, and using a novel brain imaging technique to investigate the role of amino acid neurotransmitters in depression.

Dr. Hegadoren hopes her work will produce intervention strategies that consider both the dynamic contexts of women's lives and the importance of the type of trauma to their responses to stressful life events.

Dr. Tony P. George

Clinical Director for the Schizophrenia Program at the Centre for Addiction and Mental Health (CAMH)
Endowed Chair in Addiction Psychiatry
Professor, Department of Psychiatry, University of Toronto

Dr. George is an expert in the pharmacology of drugs of abuse, co-morbid substance abuse and serious mental illness. His research focuses on the cognitive neuroscience of addictions and treatment of tobacco addictions in special populations. Dr. George's work involves understanding all the elements that influence mental illness and addictions and to determine which comes first, a psychiatric disorder or an addiction.

JUDGING PANEL

Dr. David A. Wolfe

RBC Chair in Children's Mental Health at the Centre for Addiction and Mental Health (CAMH), Head of the Centre for Prevention Science in London
Professor, Department of Psychiatry and Psychology, University of Toronto
Editor-in-Chief of Child Abuse and Neglect

Dr. David Wolfe is a psychologist and author specializing in issues affecting children and youth. Dr. Wolfe has broad research interests in abnormal child and adolescent psychology, with a special focus on child abuse, domestic violence, and developmental psychopathology. He has been pioneering new approaches to preventing many societal youth problems such as bullying, relationship violence, and substance abuse. His research team developed and evaluated the school-based 'Fourth R program' to promote healthy relationships and reduce violence and abuse among youth, which is widely used across North America.

Dr. Salah El Mestikawy

Research Scientist, Douglas Institute, Montreal
Professor, Department of Psychiatry, McGill University

Dr. Mestikawy's work consists in the study of neurons using glutamate as a neurotransmitter in healthy and diseased central nervous systems. Before being released as a result of an electrical stimulus, glutamate is accumulated into synaptic vesicles by means of three specialized transporters, VGLUT1-3. These transporters are key anatomical and functional markers of glutamatergic neurotransmission. Since 2000, Dr. Mestikawy and his team have contributed to the discovery of these three VGLUTs, and have implemented a number of tools and methods to provide for new ways of studying the role of glutamatergic systems in healthy and diseased brains. He also directs an international research team based both at the Douglas Institute and at the Pierre & Marie Curie University in France.

Dr. Susan R. George

Research Scientist and Professor, Department of Pharmacology and Toxicology, University of Toronto.

Dr. George and her research team are interested in the molecular pharmacology of the G protein coupled receptors for the neurotransmitters such as the dopamine, serotonin and the opioids. Her research focuses on the regulation of receptor function, receptor homo-oligomerization and hetero-oligomerization, second messenger coupling, structure-activity relationships, and brain distribution of the receptors and mRNA. Receptor gene-deleted animal models are studied to define the specific functions of the closely related receptor subtypes, particularly as models to define the receptor systems contributing to the vulnerability to substance abuse and neuropsychiatric disease such as anxiety, depression, and schizophrenia.

Main Submission

The suburban built environment: Challenges to the mental and social health of older adults

Erik J. Bracciodieta

University of Toronto

After World War Two, North America embraced an automobile-focused urban design. Growing car ownership commanded increased residential lot size to accommodate garages, wide arterial roads and ample free parking. The parents of the Baby Boomer generation were drawn by the abundant green spaces, low residential density, and large house size of suburban living because it provided a healthy and safe place to raise children. These land developments appeared efficient, desirable and healthy.[1] However, the vision of a healthy, happy suburban lifestyle has not come to pass: suburban residents are on average 6 pounds heavier than their urban counterparts.[2] There is limited appeal for active modes of transportation in suburban areas, in part because pedestrians and cyclists are more likely to be killed in accidents.[2] Three generations later, suburbanization continues to be the predominant form of urban expansion in North America. Two thirds of Canadians live in the suburbs,[3] making urban design an important tool in health promotion.

Living in the suburbs can be unhealthy for several reasons. The heavy reliance on automobile transport can deter active modes of transportation, like walking and cycling. Social capital, or a sense of belonging to the wider community, is often lower in the sprawling suburbs, compared to dense downtown areas. This can have negative impacts on mental health.[1] With few people walking, and a lack of public meeting spaces, there are fewer opportunities for spontaneous, informal social interactions.[4] Daily suburban commutes can leave drivers too tired, depleted and irritable to build social capital, and the impulse for larger homes and private transportation (at the expense of public space) reduces people's enthusiasm for local government and public initiatives.[4] Feelings of loneliness, listlessness, and exhaustion are often the result.

Automobile dependence and the decline of social capital are particularly harmful for the suburban-living older adult. With an aging population, the issue of how citizens with varying levels of mobility engage with the built environment should be addressed. What an individual *can* do versus what one *does* do in terms of mobility is a useful framework to approach how the built environment affects social engagement.[5] What one *can* do is dependant on one's physical capabilities, which can be limited by living in a built environment that does not promote physical activity and social interactions. An older adult's daily functioning can be reduced if they develop an impairment or disease process that limits their ability to drive. Suburban-living older adults may also be limited in terms of their social interaction and opportunities to interact with the environment. As a result, older suburbanites are susceptible to spending increasing amounts of time alone at home by necessity rather than preference. Older adults who choose to downsize their suburban living space are often forced to leave the community due to a lack of smaller, accessible living spaces, which contributes to high residential turnover and further isolation.

The built environment also has an equal influence on what one *does* do. Wide, well maintained sidewalks, inspiring landscaping, footpaths, street furniture, outdoor public space and close proximity to nonresidential land use encourage aged individuals to leave their homes and interact with people.[6] A Florida study assessed how perceived social support was affected by the architectural details of 403 blocks in East Little Havana, a community with a large older adult population.[7] Building height matching street width, stoops, porches, high window area, low windowsill height and short building setback were found to correlate with a greater sense of social support and a lower incidence of psychological distress.[7] These design elements resulted in streets and outdoor areas that felt welcoming and encouraged residents to congregate, such as on porches, and there is a feeling of 'eyes on the ▶

street,' so aptly described by urbanist Jane Jacobs in the 1960's. A sense of security can be fostered by having people close at hand and not separated from long building setbacks and car parking spaces. Environments that promote mental health and wellbeing invite people out of their residences, increasing chance encounters between neighbours. Typical suburban environments lack these beneficial design elements, reducing the opportunity for individuals to casually interact with others. A study, among one thousand survey respondents in the Greenwich neighbourhood of London, England, found depressive symptoms significantly correlated with complaints of poor social participation due to few community events and 'not enough places to stop and chat.'[8] Increasing opportunities to develop social capital can help older citizens by decreasing symptoms of anxiety and depression.[9]

How suburban areas adapt to accommodate its aging populace may define North American urban planning in the twenty-first century. Interviews with older adults living in care facilities revealed a vision of mental health that is dependant on social interaction and physical activity.[10] Identifying and replicating the benefits of dense urban living may become a key tool for public health officers promoting healthy aging. Neighbourhoods redesigned on the principles of active transportation and casual interaction will not only benefit older adults, but also serve as environmentally sustainable and healthy habitats for people of all ages. ■

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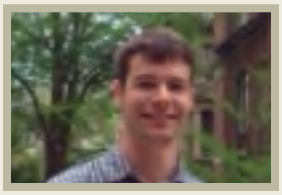

Erik J Bracciodieta

Erik J Bracciodieta is a first year Master of Biotechnology student at the University of Toronto. He studies the how basic science discoveries in molecular biology become clinical treatments with particular emphasis on the commercialization of anti-cancer pharmaceuticals. Erik is also interested in the intersection of urban design, socioeconomic geography and community health.

Main Submission

Questioning the assumption of universality in psychiatric approaches to mental healthcare in Canada

Rowan El-Bialy

Memorial University

Mental health services in Canada are primarily based on knowledge gained in the fields of psychiatry and psychology. These fields have, in turn, emerged from a very specific cultural and historical, that is, English-speaking and Euro-American, context. Over the past thirty years, scholars in cross-cultural psychiatry have examined the applicability of western psychiatric approaches to mental health in other cultures. This body of research views the knowledge system of psychiatry as a product of the culture in which it has emerged, and demonstrates that it is neither universal nor applicable in other cultural contexts. In this paper, I will examine some of the arguments that scholars in this area have put forward, while considering the implications of this research for mental health services that serve ethnolinguistic groups in Canada.

In the 1980s, Arthur Kleinman, a psychiatrist and anthropologist, argued that psychiatry is a product of western culture, and thus psychiatric categories and treatments are specific to that culture, and not universally valid. He conducted research in Asia to investigate how culture influences how one perceives mental health and illness.[1] He argued that the biomedical view of mental illness as an individual matter emerges from a uniquely western worldview, and although it makes sense to those immersed in that culture, it cannot be extrapolated to other cultures and worldviews.[1] Since then, a robust body of research has emerged that has identified several characteristics of the psychiatric approach to mental health which limit its applicability in other cultures. Two such characteristics are: the biomedical basis of psychiatry and the emphasis on mental health as an individual affair. I will briefly discuss how these two characteristics have been problematized in the literature.

Western psychiatry is undoubtedly built upon the biomedical model that underlies western medicine.[1] A good example of this is the Diagnostic and Statistical Manual (DSM)'s categorization of mental illness in terms of 'diseases' and 'disorders'.[2] Similarly, the biomedical nature of psychiatry is apparent in treatments for mental illness, which often rely on drug-based therapies. Although many accept this biomedical approach to diagnosing and treating mental illness, others who view mental health through alternative cultural and knowledge lenses reject it. For example, in a study by Laura Simich and colleagues,[3] members of five ethnolinguistic communities in Toronto expressed hesitation over using mental health services in Canada due to their relatively narrow, biomedical focus. One participant compared mental health services in Canada with those in Poland; the former focuses on ridding the individual of what is seen as a medical illness, while the latter focuses on rehabilitating the person physically, mentally, and spiritually through non-medical therapies. Similarly, scholars have argued that the medicalization of mental illness can trivialize the social problems that cause them.[1,4] In one study, refugee women who were interviewed about feeling depressed said that mental health 'treatments' should not target their individual psyches, but the structural inequalities leading to their distress.[5] These examples demonstrate how the biomedical approach to diagnosis and treatment of mental health problems limits its compatibility with alternative understandings of mental health.

The psychiatric approach to mental health is not universally applicable for another reason: it focuses almost exclusively on the individual as a locus of diagnosis and treatment.[6] In many social contexts, however, a person's identity is not experienced so much as an individual identity, but as a part of a collective or a group.[7] In such cases, the individualized psychiatric approach to mental health would be inappropriate because it does not address the social causes of mental health problems either in diagnosis or treatment.[5,6] In response, alternative approaches to mental health have been developed that focus on promoting ▶

community mental health, with particular attention to social experiences that are shared among community members and impact their mental wellbeing.[6] Such programs seek to strengthen the community's existing networks and sources of resilience, as well as addressing social inequalities that make community members vulnerable to mental health problems. Community mental health promotion projects have been successfully used in different types of communities, such as groups of immigrant and refugee women from diverse cultural backgrounds,[8] as well as communities recovering from tragic events.[9]

Although many people who suffer from mental health problems find the western psychiatric approach to diagnosis and treatment beneficial, this approach is not universally applicable to people who have alternative understandings of mental health. Alternative knowledge of mental health can be found amongst diverse ethnocultural groups, who may hesitate to use current mental services because they are not compatible with their own understandings of mental health. In a country as diverse as Canada, it is critical for policy makers and service providers to acknowledge alternative ideas about mental health, in order to develop services that do not systematically exclude ethnocultural members of the population. Greater effort should be made to learn about alternative understandings of mental health, without automatically recoursing to the categories and treatments of mental illness created by western psychiatry. ■

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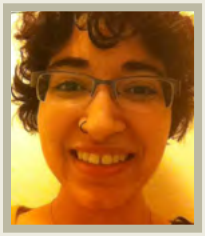

Rowan El-Bialy

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Main Submission

Mental health courts: The key to decriminalizing the mentally ill?

Andrea Ennis

Acadia University

The deinstitutionalization movement of the late twentieth century saw vast closures of psychiatric hospitals. Despite intent to redirect patients towards community-based treatment, mental health services became progressively scarce. Many of those without access to adequate services were criminalized and increasingly became the responsibility of the criminal justice system, and prisons became surrogate psychiatric facilities.[1] Overall rates of mental disorders among inmates vary; however, the average is around 16% for men and 31% for women;[2] a rate that has steadily increased by approximately 10% per year over the past two decades.[3] The increasing complexity of offender profiles and escalating need for mental health services places a strain on an already overburdened correctional system, leading to decreased access to mental health resources and unresolved issues that can elevate risk to reoffend. To halt this "revolving door",[4] Mental Health Courts (MHCs) have been developed.

MHCs are problem-solving courts, in which judicial alternatives that promote wellbeing are employed in place of traditional criminal sanctions.[5] MHCs strive to reduce the number of mentally ill in prisons by diverting them to community-based rehabilitative treatment. MHCs thus revisit a goal of deinstitutionalization – connecting clients with mental health services in the community. Critics argue that governments have turned too readily to MHCs as a quick, visible solution, compounding the problem by ignoring substantial gaps in community services.[6] Priority should be placed on 1) crime prevention, by addressing root causes of criminalization; and 2) revamping the civil mental health system. However, MHCs are a necessary part of a solution to decriminalize the mentally ill, as measures must be in place for them when they find themselves in contact with the law. Police initiatives that connect individuals with mental health agencies in lieu of pressing charges are a key interim step, and for those charged, MHCs provide another line of defense in decriminalization efforts.

Structure of Mental Health Courts

MHCs emerged in the United States in the mid-1990s. Canada was quick to follow suit, with MHCs established in most Canadian provinces, although primarily in urban centers. As MHCs are a relatively new phenomenon, they may not be well understood, and to complicate matters, there are various models that identify as an MHC.[4] Most MHCs are comprised of a collaborative and multidisciplinary team who provide mental health services and connections to community resources.[7] In contrast to the regular court system, MHCs operate like a program, where in addition to the full-range of sentencing options, judges oversee the provision of treatment services, while also monitoring and imposing sanctions for non-compliance with the treatment plan and court-imposed conditions. Often, potential candidates are identified through the regular court system and presented with the option of transferring their charges to the MHC. Their decision to do so is voluntary; they either consent to participate in treatment through the MHC with the possibility of dismissed charges or a reduced sentence given compliance with the MHC program, or proceed through the regular court system. MHC eligibility varies extensively; some accept only those with a primary Axis I diagnosis (i.e. all psychiatric diagnoses, except mental retardation and personality disorders),[8] while others accept a broader range of diagnoses. Most MHCs accept individuals with comorbid Axis I and substance abuse disorders, so long as the substance abuse disorder is *not* the primary diagnosis. Generally, candidates must have a significant and persistent mental illness that is believed to be a primary contributing factor in their criminal behavior. Eligibility also varies in terms of offence type. Some MHCs only accept those with minor offences, while others accept the full scale of offences. MHCs must also weigh mental health needs against public safety and therefore, some offences may be deemed inappropriate for diversion ▶

via MHC, particularly for violent and/or high profile cases when victim concerns or public outcry may be present.[9]

Effectiveness of Mental Health Courts

While there is certainly need for more research, the extant literature on MHC effectiveness suggests that participation in MHCs has a positive impact, leading to reductions in recidivism and alleviating strain on the correctional system. Studies in the US have found that those who successfully completed an MHC program were 22% less likely to reoffend and 50% less likely to reoffend violently compared to similar individuals processed through traditional courts.[10] Similarly, two years after MHC completion, participants had lower offence rates than in the two years prior to entering the MHC.[11] These promising results highlight the need to further research MHC effectiveness. This is particularly true in Canadian jurisdictions, as even less is known about the ability of MHCs to reduce recidivism and improve access to mental health resources. Such research would be timely, as recent legislative changes by the Canadian government have imposed "tough on crime" measures, such as mandatory minimum sentences and fewer conditional sentences for certain crimes, despite decades of research showing greater efficacy with least restrictive measures and supporting community-based rehabilitation.[12] The expected increase of the inmate population only compounds the issue of strained resources, thus underscoring the need to divert those capable and willing through an MHC program.

Decriminalization of the mentally ill begins by addressing the root causes of criminalization, such as the state of the civil mental health system. Admittedly, MHCs cannot achieve their goal of redirecting clients towards community-based services if those services are not readily available and adequately resourced. However, addressing these gaps is only the first piece of the solution, as those with mental illness are still being arrested, charged, and incarcerated at disproportionately high rates. To combat this issue, criminal justice agencies must work with government and community partners – sharing knowledge and integrating resources to make the common goal of decriminalizing the mentally ill attainable. Without the resources to offer adequate community mental health services, MHCs will undoubtedly face the same fate that was observed with deinstitutionalization – noble goals that could not fully be achieved due to lack of resources. ■

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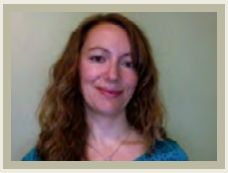

Andrea Ennis

Andrea Ennis has worked within the correctional system for the past eight years and is currently pursuing her MSc in Clinical Psychology at Acadia University. She received her BSc in Psychology from Memorial University of Newfoundland. Andrea's research focuses on the prevalence, assessment, and treatment of mental illness within the criminal justice system.

Main Submission

An ounce of prevention would go a long way for depression in Canada

Devin Mahnke

University of Calgary

In the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR), Major Depressive Disorder (MDD) is characterized by symptoms of sadness, loss of interest, fatigue, sleep or appetite disturbance, guilt, and suicidal ideation.[1] A diagnosis of MDD is given if at least five symptoms, including sadness or loss of interest, persist for at least two weeks. Under these criteria, depression afflicts one in 10 Canadians at some point in their lives. While prevalence estimates are more variable in young people due to heterogeneity in age range and diagnostic paradigm (symptoms can present differently and be more difficult to identify in young people), a recent study indicates that depression afflicts about 8% of adolescents.[2] Despite the considerable burden of depression on youth, evidence indicates that they are presently underrepresented in mental health research and services.[3] Although numerous advances have been made in pharmacology, psychotherapy, and other therapeutic approaches, depression remains a large and undertreated burden on Canada's health care system. The prevailing discussion of depression, which includes information provided by organizations like Health Canada, focuses on risk factors outside of the individual's control, such as genetic predisposition, financial hardship, and death of a loved one.[4] It is important to acknowledge that public health may be better served by focusing on the modifiable social and lifestyle factors that contribute to MDD, in addition to acknowledging the impact of extrinsic factors.[5] Identifying and treating depressive symptoms as early as possible with a focus on preventative approaches could greatly benefit Canada's economy and the health of our population.

The small things add up, and youth in particular could benefit from increased awareness of, and emphasis on, depression-related factors within their control. This point is especially relevant considering the reluctance of young people, and their parents and healthcare providers, to use antidepressant medications as a first-line treatment for depression.[6] A host of lifestyle factors contribute to increasing risk of depressive illness, including stress, obesity, sleep deficit, lack of exercise, and social isolation.[5] Furthermore, clinical data suggest that depression is better characterized as a continuous spectrum,[1] as opposed to the clean break between depression and wellness implied by the DSM-IV. The evidence supports adopting a societal view of depression as a state strongly influenced by personal and social health, which can affect nearly anyone given the right circumstances, rather than as a disease with which certain people are afflicted. A focus on modifiable factors could provide symptom abatement and quality-of-life improvement for some sufferers of depression,[5] improving public health overall and leaving the healthcare system to intervene only when it is truly needed.

The lion's share of the study and treatment of depression goes to adult populations, but the disorder is relatively more prevalent in youth,[3] being one of the chief causes of disease burden in individuals aged 15-24.[6] Successful treatment of adolescent depression not only serves to alleviate suffering and risk of suicide in young people directly, but could also curb the incidence of continued mental illness, alcoholism, and drug abuse stemming from unresolved depression.[6] Considering childhood or adolescent depression is a strong determinant for continued mental illness and substance abuse incidence, it is important to note that early intervention in young people may potentially be more impactful than similar intervention in adults. Furthermore, recent epidemiological research supports a 'staging model' of mental illness, by which more serious disorders can potentially be predicted by subclinical symptoms of depression during adolescence.[7] From the perspective of public health promotion, addressing the mental health needs of young people stands to benefit everyone. From an economic perspective, although the cost of depression ▶

is largely manifested as lost productivity in the workforce,[8] the most cost-effective solution will be prevention of the disorder *before* entry into the workforce.[9]

In combating depression, research indicates the importance of early intervention and preventative strategies, which will require increased awareness of the importance of youth mental health as well as expansion of youth mental health services. Renowned psychiatrists Dr. Stanley Kutcher and Dr. Patrick McGorry, major proponents of early intervention strategies, argue that what is needed is a concerted effort in addressing youth mental health through specific policy changes[8] and introduction of youth-friendly treatment programs, which may be most effective if integrated into the school system.[9,10] These are sweeping changes that will require a large investment of time and effort to implement,[8] but the evidence suggests that the cost of continuing to inadequately address the mental health needs of youth would be far greater. The guidelines to improving early detection and treatment have been laid out.[7-10] What remains is to appreciate the importance of preventing depression in young people, and act on it. ■

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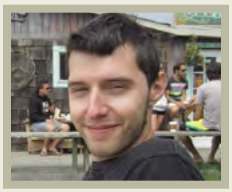

Devin Mahnke

Devin is a Master's student in Neuroscience at the University of Calgary. He is interested in understanding how mental illness affects the structure and function of the brain, and is currently using magnetic resonance imaging to study Bipolar Disorder and Major Depressive Disorder.

Main Submission

Rethinking suicide methods and motivation

Alice Muirhead

University of Northern British Columbia

Several months ago, I was speaking with a high school teacher about the difficulties many young people face when she shared the following story with me. A student had been absent from school for a few days, and when questioned, his friends replied that he had been caught vandalizing cars as part of gang initiation, was in jail, and would be back the following week. He returned the following week and attended school for several days before going missing again. This time however, he had been hospitalized for third degree burns, the result of being repeatedly dosed in body spray and lit on fire, an act that he agreed to. He spent months recovering and will carry scars for the rest of his life.

This story left me with many questions about adolescent development, the desire to belong, and how parents, schools, and communities can address self harm to support the development of strong, healthy individuals. Thinking about the story, and researching self-harm, I came to the conclusion that adolescents who have a well-defined sense of identity, rooted in knowledge of their personal, family, and community history, are able to envision who they can be in the future. With a clear idea of who they can be in the future, young people are less likely to participate in self destructive behaviour.[1-3]

The term parasuicide is used by some researchers to describe deliberate self-harm in the absence of suicide ideation, while other researchers use the term as a synonym for attempted suicide.[4-6] Using either definition, literature shows that parasuicide is a strong predictor of future suicide completion.[4-6] Therefore, I suggest that the term "parasuicide" could encompass self-harm, self-mutilation, eating disorders, and/or problematic substance use: all behaviours that indicate a lack of self-care and slow, possibly unconscious, suicide attempt. In opposition to the definition that suggests self-harm can occur with no intent to cause death, I suggest that the intent to die is present whether the individual is able to articulate the intention or not.[4] Suicides are generally thought of as lives ending quickly through hanging, suffocation, poisoning or jumping; but perhaps suicide comes in many other forms, some of them that occur more slowly.

Factors that predispose an individual for suicide include mental illness, abuse, loss of a loved one early in life and a family history of suicide.[2] In the presence of these predisposing factors, divorce, pressure to succeed, conflict with the law, financial difficulties and rejection by society are thought to contribute to the creation of crisis and precipitate suicide attempts.[2] Contributing factors, including physical illness, sexual identity issues, isolation, and an unstable family environment can also make an individual more prone to attempting or completing suicide.[2,5] These predisposing, precipitating, and contributing factors are similar, if not identical to, risk factors for self-harm, disordered eating, and substance abuse.[4]

Michael Chandler[1] argues that the question for researchers concerned with suicide should not be why do people commit suicide, but why, in the face of so many obstacles throughout our lives, do more of us not? I suggest this question can be expanded as many people experience loss, rejection, unstable family environments and various other problems without resorting to self-harm, eating disorders, or substance abuse. Research on resilience, family and social support, and participation in academic and extracurricular activities shows that young people must have a clear idea of who they are, and who they will be in the future, to act in a manner that is life-preserving, rather than self-destructive.[1-3,7-10] Having a clear idea who you are requires knowledge of your history, including the history of your family, community and culture.[1] With a clear picture of who you are, it becomes easier to imagine the person you will be, including the career you might pursue or the family you might build. I believe that, in supporting the formation of identity in adolescents parents, schools, ▶

and communities will support the existence of adolescents who care about their well-being and who are inclined toward self-preservation rather than self-destruction.

The suggestion that adolescents with a strong sense of identity are less likely to participate in self-destruction – in any form – requires further research and discussion. The potential of further research and discussion includes strong, resilient young people inclined toward self-care and self-preservation, a goal worth striving for. ■

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Alice Muirhead

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Main Submission

Tackling youth mental health inequities: Opportunities and challenges of eHealth

Johanna Sam

University of British Columbia

Mental illness is a large disease burden for youth across the globe, with mental health problems affecting 10-20% of youth in Canada.[1,2] Currently, 3.2 million Canadian youth, ages 12-19, are vulnerable to developing a mental illness, and many do not receive mental health services, such as counselling or psychotherapy.[2] Moreover, research shows that mental health promotion initiatives, such as educational resources promoting healthy behaviour, can strengthen personal wellbeing with concrete, positive outcomes for youth.[2] As young Canadians integrate online activities into their lives, the use of the Internet, computers, mobile phones, and related technology offers an innovative and cost-effective opportunity to engage youth in mental health services and promotion.[1] eHealth is an emerging field, which brings together the use of technology, the coordination of online health systems, and the delivery of health services and promotion.[1] The present paper considers the potential for eHealth strategies to advance accessibility and equity of mental health services and promotion for youth.

Ongoing Needs in Youth Mental Health

Globally, youth engagement in mental health promotion and treatment is considered challenging.[3] Low utilization rates, missed appointments, and the lack of youth-friendly services frequently affect program success and health outcomes.[2] Clinicians and researchers around the world cite both social (e.g. socioeconomic status, public policies, or primary care availability) and individual (e.g. genetics or temperament) determinants that can influence accessibility and equity of youth mental health services.[3,9] In Canada, healthcare enlists eHealth services to improve access to vulnerable populations, such as videoconferencing with patients in remote communities.[5] Provinces and territories are collaborating to leverage federal resources to implement electronic health systems and policies to expedite eHealth services within primary care.[5] Similarly, a coordinated and national commitment to develop eHealth strategies is necessary to modernize Canadian youth mental health promotion and treatment.

Despite the need for reform, Canadian youth mental health accessibility remains relatively static.[2] In recent years, there have been few instances of transformative innovation in Canadian healthcare.[6] Canada's healthcare framework is grounded in both the Constitution Act of 1867 and the Canada Health Act.[6] Furthermore, the current Canadian economic condition constrains the availability of resources necessary to support "big bang" or radical, nationwide transformation in mental health care.[6] As such, incremental eHealth integration into Canadian youth mental health services is a realistic alternative to encourage nationwide changes. For example, eHealth can enable access to programs and can minimize costs by creating youth-friendly mental health mobile phone applications or utilizing social media in psychiatry to connect with outpatients (e.g., private Facebook messaging). The advancement of technology can be used to bridge the many gaps in the delivery of youth mental health services and promotion.

Contributions of Technology

With technological availability, mental health programs worldwide gradually embraced eHealth to aid in the delivery of an equitable and cost-effective youth mental health care system. The common delivery of eHealth services in many countries has been in partnership with primary care services, community services, or virtual clinics administered by specialists.[7] For example, eHealth plays a role in Australia's mental health delivery by offering several free evidence-based online self-help psychotherapy services, such as MoodGYM and BluePages.[8] These examples highlight opportunities in how eHealth could be used in Canada's youth mental health to improve health outcomes, extend services, and reduce hospital readmission ▶

rates.[8] These eHealth services could potentially address social determinants of health among young people.

eHealth programs have the potential to reduce mental health inequities experienced by youth. Internationally, researchers indicate that social factors, such as distribution of health resources or socioeconomic status, influence accessibility, equity, and health outcomes of these programs, as stated above.[9] To tackle these social determinants, study findings show that universal school-based mental health programs, administered by teachers, assist in addressing health inequalities.[10] These programs offer computer access to the entire student population in order to engage youth in online evidence-based modules; these modules help to overcome hardships and to connect the thoughts, feelings, and behaviours of youth.[10] Conversely, this strategy fails to reach highly vulnerable youth, such as dropouts or the homeless. Therefore, schools, primary care facilities, and community services must work together to provide multiple routes to online youth-friendly mental health programs. Moreover, these youth may require alternative technology access, such as youth centre computers, Aboriginal community centres, public library Internet services, or mental health programs that loan mobile phones.

Conclusions

Technology provides an opportunity to engage youth because a significant number of young Canadians use online applications in their daily lives. The rapidly increasing – yet largely uncoordinated – demand for technological support related to the development and deployment of eHealth initiatives highlights the need for a national strategy to accomplish these goals. Presently, public health policies do not adequately focus on social determinants influencing health among youth. Decisions to integrate technology into youth mental health services need to be given careful attention and consideration; these decisions require policy direction. The resulting strategic integration of technology into these services will help improve accessibility and youth engagement in mental health promotion and treatment and, in so doing, will ensure that our youth attain the best quality of life possible. ■

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Johanna Sam

Johanna Sam is a proud member of Tl'Etinqox T'in Nation. She is currently completing her Master of Science degree in Population & Public Health at the University of British Columbia. Her research project is guided by attachment theory to examine gender differences in the relationships between adverse childhood experiences and whether attachment style is related to ways in which youth access mental health services – especially mental health services that are being delivered or facilitated by new technology. Her interests involve new information and communication technology initiatives designed to enhance equity for socially marginalized populations, such as Indigenous people, youth, and women.

Main Submission

Solutions at the doorstep: Reflections on physical contact with nature for mental wellness

Renate Sander-Regier

University of Ottawa

Nature has been characterized as a valuable and versatile health resource,[1] with therapeutic value yet to be fully realised.[2] Contact with nature has been described as a mental health strategy that is cost-effective, widely accessible, clinically valid, and free of adverse side-effects.[3,4] Access to green space has even been cast in terms of a mental health "necessity."[5] If, as predicted, depression will become the second greatest cause of ill health globally by 2020,[4] the potential value of nature to mental health may warrant serious consideration.

A recent review of emerging research[5] reveals the extent to which contact with nature can benefit mental health and vitality. Beneficial contact can range from simple exposure to a green view through a window, to active walking among trees, to engaged hands-on work with plants. Such contact can yield a wide range of benefits, including reduced levels of the stress hormone cortisol, rapid and more complete recovery from stress when it occurs, lower blood pressure and pulse rate, higher alpha wave activity, and both cognitive restoration and better cognitive performance.[5]

A University of Essex (UK) research program focuses on the effects of green exercise, defined as "physical activities in nature."[6] Results from carefully controlled laboratory simulations demonstrate that exercise in natural outdoor locations is more effective at improving physical and mental health than exercise in other places, or than physical exercise alone. Green exercise is described in terms of synergistic benefit, with the key to the synergy being the green, outdoor setting of the physical activity.[7]

Studies commissioned by the English and Welsh mental health organisation MIND have confirmed this synergy. A summary of results indicates a 71% decrease in depression levels after outdoor walks, compared to 45% after equivalent indoor walks; a 71% reduction in tension after outdoor walks, compared to 28% after indoor walks; and a 90% increase in self-esteem after outdoor walks, compared to 17% after indoor walks.[8] One research participant said, "My fitness has improved, I feel refreshed and alive."[4]

Evidence also indicates higher rates of adherence to green exercise regimes[1,5] – one reason why a program called "Green Gym" is increasingly being prescribed by UK general practitioners.[9]

Compelling Potential

The "Green Gym" program is managed in the UK by The Conservation Volunteers (TCV), a national organization which coordinates volunteer activities to help maintain urban green spaces and rural natural areas. Volunteers work in teams to perform a range of activities including planting trees, creating community gardens, managing local woodlands, and maintaining public footpaths.[4] TCV and local MIND groups are working together to develop nearby Green Gym programs to help people experiencing mental distress.[4]

The UK's Royal Society for the Protection of Birds (RSPB) is another organization that offers opportunities for physical outdoor conservation activity. One volunteer, who suffers from epilepsy and Asperger's syndrome, speaks of experiencing unemployment and depression that plunged him into "a very dark spell". Family and friends urged him to volunteer at a local RSPB nature reserve, and he has been working there for three years, performing various physically demanding tasks that he credits with building up his strength and his mind.[2]

"Tasks like digging holes are a real source of stress relief and act as a therapy," he says. "I can also feel myself getting fitter and stronger and this all adds to my confidence." He declares that nature volunteering has changed his outlook completely, giving him a new focus and helping him feel ▶

better both mentally and physically[2] – a powerful testimony to the benefits of physical engagement with the natural world.

Green exercise for mental health in Canada?

In Canada, no national version of the UK's TCV exists to coordinate outdoor conservation volunteering. Neither does Canada's MIND equivalent, the Canadian Mental Health Association (CMHA), appear to promote contact with nature or outdoor physical activity as discernible strategies for protecting and improving mental health.

Nevertheless, opportunities exist for local CMHA branches, mental health practitioners, and other interested parties to coordinate with regional partners to develop green therapeutic interventions literally at the doorstep. Community and botanical gardens, for example, offer opportunities to work with plants and soil in the outdoors. "Friends of ..." local parks groups often seek volunteers to work at local protected areas. Regional walking and hiking clubs organize guided outings, while field naturalist and birding groups coordinate field trips. Many of these groups are active during the winter with monitoring ski and snowshoe trails, tending plants in greenhouses, or exploring the snowy landscape at a time of year when weather conditions tend to limit outdoor exercise opportunities. ■

Physical activity in green settings is increasingly being proposed as a cost-effective and widely accessible intervention which can make significant contributions to protecting and enhancing mental wellness. While Canada lacks a national green therapeutic intervention network, opportunities exist to develop fruitful partnerships and solutions close to home, perhaps even growing to national proportions with time.

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Renate Sander-Regier

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Main Submission

Staying mindful: Lived experience and mental health care reform in Canada

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University of Victoria

"We get [mental health] consumer representation on our committees and boards and then snow them under with bureaucratic paper and administrivia. We burn them right out and then we cluck sadly and whisper that they weren't really up to it after all. Their medication needs adjusting, we say, and we are really so damn sympathetic."[1]

A Decade of Momentum

In the past decade, mental health and mental health care have become increasingly popular issues in Canada due to provincial, federal and private sector investments in mental health promotion and treatment, and the growing visibility of the consumer and caregiver movement throughout Canada. From 2005-2012, seven provinces and one territory introduced mental health strategies, and the first national *Mental Health Strategy for Canada* was released by the Mental Health Commission of Canada in 2012.[2] These developments have heightened the profile of mental health across Canada, and have provided momentum for new consumer-informed, privately funded public education campaigns such as *Partners for Mental Health* that works to reduce the stigma associated with mental health problems and accessing mental health care.[3]

While these were important milestones in Canada's history of mental health services, the momentum would not have been possible without the work of thousands of Canadians with lived experience.[4] Canadians with lived experience include any person that has had some experience with mental health, mental illness or mental health care, including consumers of mental health services, and family members and caregivers of persons with mental health problems. To ensure the success of current and future initiatives aimed at reforming mental health services, this paper argues that it is imperative that policy development be led and informed by the perspective of persons with lived experience throughout Canada. Involving persons with lived experience in the policy development and implementation process will better ensure that policy reforms promote a consumer-focused system of care and recovery model of treatment. The ongoing involvement of persons with lived experience in health care reform can also enhance transparency and accountability in health care service management; improve the quality and effectiveness of services, and provide legitimacy and creditability to new investments or policy directions.[5-7]

Conceptualizing Engagement and Barriers to Meaningful Involvement

The perspective of persons with lived experience can be obtained though consultation, participation, and engagement in relation to direct service delivery and treatment, in addition to service system planning and policy development.[7] The ladder of citizen participation has been conceptualized as a continuum. At one end of the continuum is information dissemination and consultation, where participants are given an opportunity to express their perspective, but there is no commitment to ongoing involvement or using the information gathered to develop policy or programs.[8] On the opposite side of the continuum is full engagement where there is an ongoing commitment to participants to use the information gathered to develop policies or services and continually involve them in the policy development process.[8] Engagement of persons with lived experience is the optimal approach for including consumers, family members, and caregivers in the policy development process because there is a clear commitment to ongoing participation that helps build trust between participants and staff. Although the engagement of persons with lived experience is the optimal approach for authentic engagement, it has not been used ▶

consistently in the development of mental health strategies throughout Canada. Most provincial and territorial mental health strategies have used online surveys, town-halls, or discussion groups to gather feedback from persons with lived experience on particular policies, programs or approaches under consideration with no ongoing commitment to continuous engagement. Planning committees composed of persons with lived experience with ongoing terms of reference have been less widely used to inform policy development; however, those that have been created have been influential in shaping the focus of policy documents such as *Toward Recovery and Wellbeing: A Framework for a Mental Health Strategy for Canada*.[9]

There are several individual and organizational level factors that inhibit authentic engagement that must be addressed if persons with lived experience are to be meaningfully involved in the development and implementation of mental health care reform in Canada. Persons with lived experience must individually balance competing demands on their time, such as caregiving responsibilities, as well as feelings of apathy related to participation, and a lack of information on engagement opportunities and research and policy development techniques.[7,8] Organizations must address significant barriers that negatively influence engagement efforts such as stigma towards persons with mental health problems; power imbalances among staff and participants; unhealthy work environments and work cultures, and financial and resource limitations.[5,7] The redistribution of power in the policy development process and competing political demands must also be addressed within organizations to enhance the success of engagement initiatives. Within engagement exercises themselves, the barrier of scientific knowledge being privileged over lived experience of mental health issues must also be actively acknowledged and managed in order to create an equitable foundation for all knowledge to be valued in the policy development process.[5]

Enhancing Engagement in Mental Health Care Reform

Enhancing the engagement of persons with lived experience in mental health care reform requires that governments, regional health authorities, and others involved in the delivery of mental health care, make a commitment to inclusive planning, policy development, and priority setting in partnership with consumers, caregivers and family members. These efforts would be strengthened by encouraging the recruitment of traditionally under-represented populations such as Aboriginal peoples, youth, young caregivers, immigrants, refugees and ethno-cultural groups on planning committees. Similarly, promoting the employment of persons with lived experience in mental health related organizations and government departments may also assist these efforts.[6,8,10] The creation of a national policy and practice collaborative focused on evaluating engagement frameworks, and building the research evidence related to optimal methods for including persons with lived experience in the policy development process, could also assist in building capacity within the health sector to promote knowledge exchange and authentic engagement with persons with lived experience. Partnerships between government departments and organizations that have a strong history of engaging persons with lived experience should be encouraged to reduce the need for departments to reinvent existing infrastructure and programming. Engagement in mental health care reform could also be encouraged by including consumer, caregiver and family member involvement as a criterion for obtaining government funding for mental health related research projects by organizations such as the Canadian Institutes for Health Research.

Conclusion

In recent years, there has been an historic focus on mental health and mental health care in Canada. Building on this momentum, it is critical that we remain mindful that persons with lived experience of mental health issues should be included and engaged within the policy development process to ensure a recovery-oriented focus. Organizations and government departments must be reflective and creative in designing engagement strategies, as well as look inward to evaluate whether their work environments are really inclusive and supportive of persons with lived experience to bring mental health '*out of the shadows at last*.'[4] ■

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Main Submission

Mind and the city: The association between urban living and schizophrenia

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In the past sixty years, our social landscape has changed at an unprecedented pace. Prompted by the rapid growth of industry, improved transportation, and alterations in economic structure, we have transitioned from a rural-centred to urban-centred society. In 1950, less than one third of the world lived in cities, whereas today, over half of the population reside in urban areas, and by 2050, this number is projected to reach 70%.[1] Although urban dwellers are usually wealthier and have better nutrition and easier access to health care services compared to their rural counterparts, the effect of urban living on mental health appears to be largely negative.[3] Specifically, the urban environment may be a crucial stimulus in promoting schizophrenia, a debilitating neuropsychiatric disorder characterized by chronic or recurrent psychosis.[2]

Epidemiological studies beginning in the 1990s, and their subsequent meta-analysis, uniformly suggest that the incidence of schizophrenia in urban areas is two-to three-fold higher than rural areas.[3-5] These studies address a wide range of possible confounders such as age, sex, ethnicity, drug use, social class, and family history, but none of these are able to explain this striking association.[3] More importantly, one third of all such research reveals a "dose-response" relationship between the number of years lived in urban areas and an increased risk of schizophrenia.[6] Naturally, an important question that emerges from these epidemiological studies is whether the association between urbanicity and schizophrenia is correlative or causal. For example, an alternative explanation is that urban dwelling is not causing the increased prevalence of schizophrenia, but instead, individuals genetically at risk of the disease tend to reside in urban areas. Although not yet definitive, current evidence suggests this hypothesis is unlikely to account for the major part of the association.[3] First, studies that adjusted for genetic predisposition of schizophrenia only found slightly reduced associations with urbanicity.[3] Furthermore, early exposure to urban environment during upbringing is associated with a higher risk of schizophrenia in adulthood, even after the individual is removed from urban centres.[7,8] Taken together, these results suggest that not only the association between urbanicity and schizophrenia is likely true, but urbanicity may actually have a causal role in the etiology of this disease.

To date, the mechanism that underlies the link between urbanicity and schizophrenia remains a mystery. This is largely attributed to the enormous complexity of the urban environment and our limited knowledge in the neurobiology of the disease itself. Nonetheless, the burgeoning field of social neuroscience is beginning to shed some insights into this issue. In a pioneering work from Germany, researchers used functional magnetic resonance imaging to compare the brain's stress response between 55 urban and rural residents. The amygdala, a part of the brain that processes negative emotion, and the perigenual anterior cingulated cortex (pACC), which regulates the amygdala shows particularly interesting results.[7] Activation of the amygdala is positively correlated with the participants' city size, and activation of pACC correlated with the duration of the city habitation.[7] Importantly, the synaptic connectivity between amygdala and the pACC is diminished in individuals from urban areas compared to rural areas, indicating a potential of reduced inhibition of the amygdala.[7] Therefore, the increased incidence of schizophrenia among city dwellers may be caused by an overly-active stress response in the brain. Consistent with this, individuals that encountered stressful experiences, such as childhood trauma or social defeats had an increased risk for developing schizophrenia.[9] It is conceivable that the relentlessly stressful city environment, with insults such as overcrowding, high crime rates, heavier pollution and noise, over time, can cause in aberrant alterations in the stress signaling pathway, contributing to the increased incidence of schizophrenia.[10] ▶

As we continue to move forward in the age of global urbanization, the task of understanding the link between city environment and mental health is increasingly urgent. Megacities in developing countries such as China, India and Brazil are growing at lightning speed and the cost of care for mental health is rising. Pinpointing the factors in urban environments that contribute to schizophrenia may allow policy makers and healthcare professionals to implement effective interventions to prevent and combat this illness. In fact, some of our most successful attempts in reducing the global disease burden came from reducing exposure to environmental risk factors. For instance, anti-smoking campaigns reduced the incidence of lung cancer and improved sanitation has led to a worldwide decline of infectious diseases.[5] Currently, the major challenge to improve mental illness prevention with environmental measures is the lack of efficient translational strategies that can bridge basic research to the clinical and population level. Greater multidisciplinary collaboration between diverse fields such as psychiatry, neuroscience, genetics, and social sciences is necessary to delineate and curtail the effect of urbanicity on schizophrenia. ■

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Main Submission

Battling bullying: Do obese children face the same fight?

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Over the past three decades, the prevalence of childhood overweight and obesity in Canada has nearly tripled.[1] While the relationship between these chronic conditions and related physiological co-morbidities has been examined extensively, less attention has been focused on the psychological and social implications of increased adiposity. Given that obesity has been shown to serve as a determinant of mental health issues in childhood,[2] additional attention is required. The following paper will address the impact of social stigmatization and discrimination, specifically bullying, on the psychological wellbeing of obese children, and will highlight potential solutions from a population health perspective.

Overweight/obese children: A "bigger" target for bullying and mental illness?

Obesity often lends way to overwhelming social calamity among children, with peer rejection being of particular note.[2] Compared to their non-overweight counterparts, obese children have greater relative odds of being diagnosed with a psychiatric problem,[3] and are at a marked risk for the development of mental health issues such as low self-esteem and poor body image.[4,5] Higher rates of anxiety, depression, and eating disorders are common among this unique population.[4]

Bullying among obese children: Adding more fuel to an already roaring fire

Although bullying has been cited as a social repercussion of obesity, the degree of bullying is positively correlated with weight (i.e., the more overweight the child, the more intense the bullying episode).[6] In fact, overweight and obese children are 10% and 60% more likely to be bullied than non-overweight and non-obese children, respectively.[7]

Even more alarming, obese children are at an increased risk for suicidal behaviours. Eaton and colleagues determined that weight-based teasing and victimization were positively associated with suicidal ideation and increased likelihood of suicide attempts among Caucasian, Hispanic, and Black students as compared to average-weight peers.[8] This finding was further evidenced by Eisenberg and colleagues in 2003, as a sample of over 4,000 children who were teased about their weight were 2-3 times more likely to report suicidal ideation as compared to those who were not teased.[9] Fortunately, there is also research to suggest that bullying and its associated suicide rates can be significantly reduced by implementing bullying education and prevention programs. In fact, children who participated in a suicide prevention program were 37% less likely to attempt suicide as compared to a control group.[10]

Battling bullying: What can be done?

Bullying is a complex social issue, and similar to obesity, there is no 'easy fix'; comprehensive interventions that include multiple sectors need to be considered. Interim steps should be taken to correct this pervasive form of social interaction. Specifically, because obese children are at increased risk of bullying, additional measures – be it social skills development, curriculum, and/or school policies – should be taken to protect their social and mental wellbeing. Firstly, healthy relationships should be promoted at home and at school. Opportunities for positive relationship building for school-aged children can be achieved through presentations and hands-on workshops which focus on empathy, help-seeking behaviours, and problem solving and reporting skills. Secondly, negative stereotypes regarding obesity (e.g., *obese people are lazy and/or unattractive*, etc.) should be addressed. Given that bullying of obese children can be partially attributed to the 'other' children's negative associations with obesity,[8] efforts should be made to correct these false perceptions. ▶

Lastly, parents and school officials play an important role in creating safe and healthy environments for children. If pro-social behaviours are displayed and encouraged by trusted authority figures, it is likely that children will mimic these actions and feel comfortable in seeking help. By working collaboratively to address bullying, thus decreasing the incidences that obese children are subjected to negative situations, we can strengthen our efforts in sheltering children from the unnecessary burden of mental health problems.

Bullying: Future directions for promoting mental wellness among obese children

Weight-based discrimination is as concerning as, for example, racial discrimination, gender discrimination, and/or discrimination against children with physical disabilities. Addressing this issue is of equal importance for the purpose of protecting the emotional and physical well-being of our nation's children. Although more work is needed to better understand the extent to which stigma and teasing increase vulnerability to suicidal behaviours in obese youths, the current findings are sobering; they highlight the critical importance of studying the impact of stigmatizing experiences on the emotional well-being of this population as well as their effects on adverse psychosocial outcomes for obese children that may be exacerbated by weight bias. Like many health-related behaviours, mental health problems tend to persist throughout the lifespan if they are not addressed early. By means of promoting mental health wellness and pro-social behaviours among all young Canadians – inclusive of those who struggle with obesity – we can strive to instill positive relational values in children as well as eradicate the weight-based stigma faced by obese children before it consumes their lives. ■

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Picture not provided.

Leigh Vanderloo

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Main Submission

Depression, diabetes, and dementia: Is there a role for insulin?

Danielle S. Cha

University of Toronto

Cognitive deficits are increasingly being recognized as a consistent, non-specific, and clinically significant feature across neuropsychiatric and metabolically-based medical conditions.[1-3] Moreover, converging evidence suggests that individuals with comorbid neuropsychiatric (i.e., major depressive disorder and Alzheimer's disease) and/or metabolically-based medical conditions (i.e., type II diabetes mellitus and major depressive disorder) are at elevated risk for hastening the progression of cognitive decline and neurodegeneration.[2,3] The phenotypic and neurobiological overlap between frequently co-occurring neuropsychiatric disorders and metabolically-based medical conditions suggests the possibility for shared pathophysiological mechanisms.[4] However, relatively few reports have aimed to describe potential mechanisms underlying the relationship between major depressive disorder (MDD), type II diabetes mellitus (T2DM), and Alzheimer's disease (AD).

MDD, T2DM, and AD are among the most common disorders worldwide and represent major public health concerns.[5] It has been amply documented that MDD represents both a risk factor and a prodrome for AD.[6] Moreover, cognitive impairments are reported to be a common and persisting abnormality among individuals with MDD.[6] For example, it was reported that individuals with MDD experience decreases in memory by approximately 2-3% following each major depressive episode.[1] Furthermore, evidence suggests that an estimated 10-15% of AD cases are attributable to depression and a 25% reduction in depression prevalence would result in approximately 830,000 fewer AD cases worldwide.[6] Conversely, approximately 20-30% of patients with AD have been reported to suffer from MDD.[6] In keeping with this view, individuals with T2DM are reported to be 52% more likely to develop MDD when compared to the general population.[5] Moreover, T2DM has been reported to significantly and independently increase risk for AD by 39% when compared to the general population.[5] These foregoing observations indicate that the cognitive changes that occur in a subpopulation of individuals with MDD and T2DM are progressive, suggesting the potential for shared pathophysiological substrates between MDD, T2DM, and AD.

Disease modeling in neuropsychiatric disorders and metabolically-based medical conditions indicate that abnormal central insulin signaling is implicated in alterations of neuronal integrity and function, affecting synaptic signaling and discrete neural circuits.[4] Replicated evidence indicates that cross-talk between central and peripheral insulin is critical to elucidating the relationship between metabolic disturbances (e.g., insulin resistance) and neuropsychiatric disorders (e.g., MDD and AD).[4] Taken together, the role of insulin in normal and abnormal peripheral and central nervous system (CNS) functioning provides a framework for characterizing its contribution to the pathoetiology, progression, and potential treatment of MDD, T2DM, and AD.

Recent interest in insulin signaling and its relationship with disorders affecting cognition is associated with its critical role as a neuropeptide, exerting pleiotropic effects involved in neurotrophism, neuroplasticity, and neuromodulation.[4,7] Insulin derived from the pancreas is transported via a saturable, receptor-mediated process across the blood brain barrier (BBB) to prompt the insulin-mediated signaling pathways involved in brain bioenergetics, reward circuits, as well as the regulation of normal emotional and cognitive brain functions.[4,7] Furthermore, insulin signaling in the CNS has been reported to prevent the pathological binding of amyloid beta (Aβ) oligomers by up-regulating the expression of insulin degrading enzyme (IDE), which also degrades Aβ.[3,4,7]

Chronic insulin-resistance related hyperinsulinemia results in the down-regulation of insulin receptor expression ▶

along the BBB impeding the transport of insulin into the brain, and chronically reducing IDE levels.[3,4,7] For example, peripheral insulin resistance has been associated with both T2DM and MDD.[3,4,8] Moreover, emerging evidence suggests that Aβ peptides may play a distinct role in depression etiology in addition to its interaction with AD pathology.[9] Taken together, the relationship between insulin, its relevant signaling pathways, and Aβ may represent a potential mechanism through which impairments in affect, cognition, and metabolic health may synergistically perpetuate neurodegeneration via separate but related systems, further elucidating the pathoetiological link and progressive relationship between MDD, T2DM, and AD.

Available evidence provides the impetus to further refine potential mechanisms and molecular pathways subserving these disorders in order to more effectively treat these populations by aiming to reduce and prevent cognitive impairments and decline, and downstream neurodegeneration. For instance , the administration of intranasal insulin has been reported to improve memory and measures of mood (e.g., depression, self-confidence, overall feeling of well-being) in healthy individuals as well as individuals with AD.[10] Notwithstanding accumulating evidence for the relevance of cognitive dysfunction in MDD and T2DM, robust therapeutic interventions specifically targeting cognitive dysfunction across neuropsychiatric disorders and/or metabolically-based medical conditions are not currently available, largely due to a paucity of empirical evidence. Thus, investigations that aim to examine the contribution of various effector systems and molecular pathways that converge across these clinical populations may provide the basis for novel treatment avenues specific to ameliorating and preventing cognitive dysfunction and thereby AD. ■

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Danielle S. Cha

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Main Submission

To die or not to die: Calpain drives Alzheimer's Disease and cancer progression

Stacy Visser-Grieve

Queen's University

It's inevitable: we will all age; we will all grow old. And we all know the characteristic signs of aging: wrinkly skin, loss of hearing, loss of memory, and increased risk of acquiring certain diseases. Two of the diseases commonly associated with aging are Alzheimer's disease (AD) and cancer. Interestingly, studies show an inverse relationship between the development of cancer and AD, such that patients suffering from dementia often have a decreased occurrence of cancer.[1] Although at first this may seem surprising, in fact, the mechanisms mediating progression of these diseases are inherently connected. In particular, each disease originates from a defect in programmed cell death, or apoptosis. Whereas AD results in neurodegeneration from enhanced cell death, cancer is often associated with pro-survival or anti-apoptotic effects. Importantly, the protease calpain plays a pivotal role in modulating both pro- and anti-apoptotic functions depending on cellular context[2] and thus may act as a driver in the development of Alzheimer's disease and cancer.

Calpain belongs to a family of intracellular Ca^{2+}-activated cysteine proteases – proteins that proteolyze or cleave their substrate proteins. Of the 14 mammalian isoforms, calpain 1 and calpain 2 (herein referred to collectively as calpain) are ubiquitously expressed and the most extensively studied.[3] By cleaving its numerous substrates into smaller functioning fragments, calpain modulates many cellular phenotypes including cell cycle progression, adhesion, migration, and survival. Due to its essential role in maintaining cellular homeostasis, the activity of calpain is tightly regulated. Primarily, Ca^{2+} binding activates calpain by allowing for conformational changes that enhance cleavage of available substrates. Alternatively, binding of the endogenous inhibitor calpastatin prevents proteolytic activity.[3]

Several studies show that calpain expression is upregulated in specific cancers, including colorectal, breast, or prostate cancers, and it may correlate with poor progression.[4] These studies suggest that calpain primarily plays a pro-tumorigenic role. Similarly, calpain also promotes Alzheimer's disease. By examining the brains of AD patients, calpain was shown to be hyperactivated due to increased levels of Ca^{2+} and/or decreased expression of calpain's endogenous inhibitor calpastatin.[5]

The ability of calpain to mediate either pro- or anti-apoptotic functions may explain how increased calpain activity can promote AD and cancer. Firstly, in AD, increased calpain activity occurs early and therefore contributes to multiple aspects of neurodegeneration. In addition to contributing to the formation of clinical hallmarks – such as senile plaques containing beta amyloid (Aβ), and neurofibrillary tangles composed of hyperphosphorylated microtubule associated protein tau – calpain also directly activates cell death pathways in neurons.[2,5] Specifically, calpain decreases activity of anti-apoptotic proteins such as Bcl-2 or activates pro-apoptotic proteins including p53 and Bax.[6] Increased calpain activity enhances cleavage of amyloid precursor protein into Aβ, contributing to the formation of Aβ plaques. Additionally, calpain specifically cleaves kinases such as GSK-β and CDK5, enhancing their ability to phosphorylate tau, leading to neurofibrillary tangle formation. Finally, calpain specifically cleaves tau into smaller fragments that signal the induction of apoptosis.[5,6] These are some examples of how increased calpain activity in the brain can lead to neurodegeneration. These changes in neuropathology potentiated by calpain inevitably lead to the loss of neurons, shrinkage and loss of neuronal processes, and dramatic loss of brain volume observed in AD patients.

In contrast with AD, tumorigenesis involves the overgrowth of cells resulting from increased cell cycle progression and/or loss of programmed cell death. In this disease setting, evidence is emerging that calpain promotes cell ▶

survival. For example, in breast cancer cells, loss of calpain 2 expression leads to reduced activity of the pro-survival kinase AKT.[7] Furthermore, loss of both calpain 1 and 2 increased starvation-induced cell death, and it also reduced activity of the AKT survival pathway.[8] Similarly, increased expression of calpain has been associated with resistance to certain drugs, including the targeted therapeutic Herceptin in breast cancer.[9] These results provide a novel hypothesis that calpain may play a pro-survival function in cancer cells as opposed to an anti-apoptotic role in normal cells.

If this hypothesis holds true, calpain could be an important therapeutic target for both AD and cancer. Using an AD mouse model, Medeiros et al recently showed that treating transgenic AD mice with a calpain inhibitor could reduce accumulation of Aβ plaques, decrease tau phosphorylation, and improve cognitive function.[10] Similar studies using calpain inhibitors in cancer settings showed how inhibiting calpain enhanced cell death in cancer cells[11] or downregulating calpain 2 expression reduced tumor growth in mouse models.[7]

Calpain drives progression of either Alzheimer's disease or cancer through its pro- and anti-apoptotic effects, respectively. Understanding the cellular context and the substrates through which calpain acts to elicit these seemingly opposing roles are current research areas garnering interest by scientists in both the AD and cancer fields. If calpain can manipulate its functions depending upon cellular context and available substrates, the question follows: are other diseases also driven by calpain? ■

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Stacy Visser-Grieve

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Main Submission

Barriers to the diagnosis of affective disorders in Parkinson's Disease

Sara Grace Lutz

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In 1817, Dr. James Parkinson[1] documented the condition of 'shaking palsy,' which was later coined as Parkinson's disease (PD). Parkinson's[1] description of 'involuntary tremulous motion' and 'lessened muscular power' came to classify the disease into a group of cardinal motor symptoms, particularly tremor, bradykinesia, rigidity, and postural instability.[2] Parkinson, however, did not consider PD to be a disorder affecting movement alone. Parkinson's[1] well-known description of one case, '[a] more melancholy object I never beheld,' provided recognition of the affective complications that can occur in PD and demonstrated the level of severity such symptoms can reach.

Despite this early identification of affective symptoms (e.g., depression, mania, anxiety, and panic) as a possible comorbidity of PD, psychiatric disorders often go undiagnosed in clinical practice. This is highlighted in such findings as those by Shulman et al,[2] whose research revealed that 44% and 39% of patients with PD demonstrate clinically significant levels of depression and anxiety, respectively. In this sample of patients, however, only 21% were identified as having depression, and 19% as having anxiety, by their treating neurologists.[2] According to these results, over 50% of the time, neurologists fail to diagnose affective disorders in their patients. From such findings, it can be argued that affective disorders are a highly prevalent, yet greatly under-recognized, feature of PD. This phenomenon raises the question: why?

Perhaps the answer is that affective disorders in PD are inherently different from those in non-PD populations. This argument stems from the fact that the particular group of symptoms that make up affective disorders in PD tend to be patterned in such a way that is unique to the disease itself. In a comparative analysis of depression among PD and non-PD populations,[3] it was found that patients with PD tend to have higher levels of dysphoria, pessimism about the future, irritability, sadness, and suicidal ideation. Furthermore, patients with PD were found to have relatively low levels of guilt, self-blame, and feelings of punishment and failure, which are typically frequent in idiopathic depression.[3] When looking at the example of anxiety,[4] patients with PD tend to experience decreased levels of generalized anxiety, which is often suggested to be the most frequent anxiety subtype in the older adult population.[5] Rather, the most common subtype for patients with PD is that of Anxiety Disorder Not Otherwise Specified (NOS).[4] In this subtype, anxiety is situational, and patients often experience fluctuating levels of anxiety and panic in direct relation to fluctuations in motor symptoms and effectiveness of parkinsonian medication.[4]

Not only does the symptom presentation of affective disorders in PD tend to differ when compared to non-PD populations, but there also exists a complicated overlap between many of the common symptoms of PD and those of idiopathic affective disorders; this, inevitably, further complicates diagnosis.[6-8] Shakiness, weakness, and impaired cognition present independently within both PD and anxiety,[7] and a masked-like facial expression in a patient with PD may look identical to the manifestation of anhedonia in depression.[8]

Mere observation of patients in clinical settings may, therefore, lead to under-diagnosis of affective disorders if their presenting symptoms are mistaken for those of PD. Utilization of validated measurement tools for idiopathic affective disorders, however, might also lead to complications. Many of these measurement tools oversample from overlapping symptom domains in the construction of their items.[7,8] If used with patients with PD, the frequency and severity of the affective disorder would be skewed. For example, 78.57% of the items on the Hamilton Anxiety Rating Scale (HAM-A)[9] oversample from overlapping symptom domains, asking clinicians to rate such symptoms as muscle tension, tremor of ▶

hands, increased muscular tone, tendency to sweat, fatigability, insomnia, and weakness. In anxiety scales that possess little oversampling from these domains, such as the State Trait Anxiety Inventory (STAI),[10] items tend to be focused entirely on generalized anxiety, which is less frequent in PD. It is, therefore, clear that such measurement tools cannot be validly used with patients with PD and that the construct of affective disorders itself is inherently different in the PD population.

Perhaps a more valid approach to diagnosing affective disorders in PD is to generate measurement tools that assess facets of affective disorders that are independent of the symptoms of PD. In order to achieve this goal, future research must aim to operationalize the construct of the affective disorder under study, thereby creating an operational definition that pertains directly to individuals with PD. It is only after PD-specific affective disorders are operationalized that respective measurement tools can be generated. Once this is achieved, it can be hoped that affective disorders will be properly identified in health care settings, and, with this improved rate of diagnosis, subsequent improvements in treatment can evolve. ■

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Sara Lutz

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Main Submission

Redox imbalance and oxidative modifications of macromolecules in brain during aging and neurodegenerative diseases

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Université Laval

Alzheimer's disease (AD) and Parkinson's disease (PD) are the two most common age-related neurodegenerative disorders affecting millions of people worldwide. Although the exact underlying mechanisms contributing to degenerative changes in AD and PD are multifactorial, oxidative stress induced damage to cellular macromolecules is widely considered to play an important and central role in the pathophysiology and progression of AD and PD.[1,2] The purpose of this article is to highlight the oxidative stress-induced damages to macromolecules in brain during aging and neurodegenerative disorders.

1. Oxidative stress in the brain during aging

Reactive oxygen species (ROS), as well as reactive nitrogen species (RNS), are products of normal cellular metabolism. Aging is associated with accumulation of these oxidative-induced damages in brain, owing to an imbalance between antioxidant defenses and intracellular generation of ROS. The overall rationale of oxidative stress in aging brain is based on the following premise: (a) the brain contains high levels of unsaturated fatty acids which are vulnerable to oxidation (particularly high in 20:4 and 22:6 fatty acids); b) the brain consumes high amounts of oxygen (about 20% of the total amount used in the body); and c) the brain contains high concentrations of transition metals such as iron (Fe^{2+}) that are key catalysts of oxidative-induced damages[3] For scavenging these free radicals, cells have an extensive antioxidant system in place comprising both enzymatic and nonenzymatic substances, which is differentially distributed within various cellular compartments. Endogenous enzymes including superoxide dismutase (SOD), glutathione peroxidase (GPx), glutathione reductase (GR), catalase, peroxiredoxins, and thioredoxins can scavenge ROS, thereby mitigating their toxicity. A decline in the antioxidant enzymes with aging may compromise cellular redox homeostasis resulting in high concentrations of ROS and RNS.[4] This may further ▶

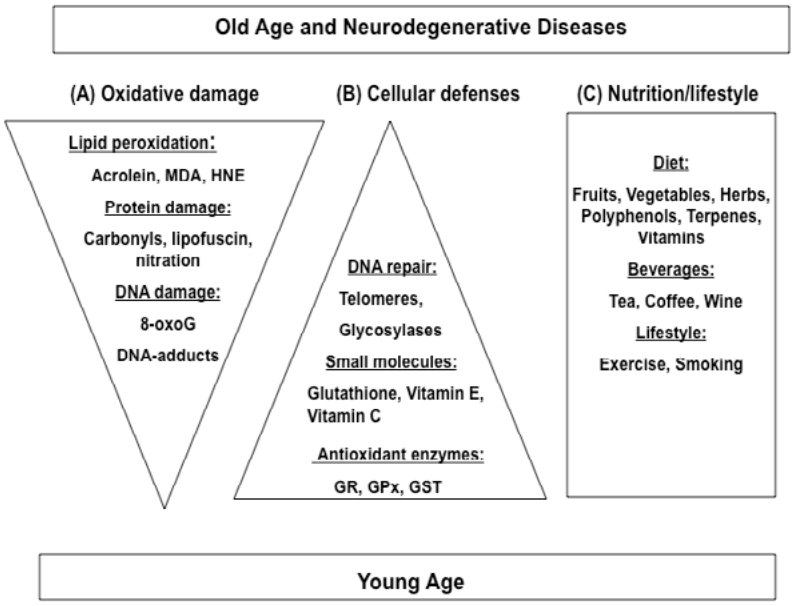

Figure 1 Interplay between cellular ROS levels, antioxidant system during aging and their modulation by nutrition and lifestyle changes. Oxidative damage increases with age, while cellular defenses decrease. An antioxidant rich diet and exercise have been shown to protect against age-related neurodegenerative diseases.

disrupt cellular redox circuits and induce damage to nucleic acids, lipids and proteins in the brain, thereby contributing to AD or PD. Although the magnitude of modifications of multiple biomolecules by oxidative damages and age-related functional losses is not a linear one, these changes are exacerbated in AD and PD as shown in Figure 1.

2. Overview of cellular macromolecule damages in the brain during aging, AD and PD

A) Protein oxidation

The most frequent oxidative modification in proteins is the formation of carbonyl groups, which may lead to inactivation, proteolysis, or formation of intra-/intermolecular cross-links. Oxidative-induced damage to proteins can affect virtually all amino acids, with sulfur-containing amino acids and aromatic amino acids being the most susceptible.[5] Protein oxidation may be considered to be the most important functionally, because proteins act as cellular receptors, transporters, enzymes, and transcription factors. In fact, the difference in oxidized proteins was found to be nearly two- and four-fold greater between young and elderly humans and rats, respectively.[6] Several carbonylated proteins have been identified in the brains of AD and PD patients. Some of these oxidized proteins such as SOD, DJ-1, and heme oxygenase-1 (HO-1) are the important components of cellular antioxidant system, and oxidation of these key proteins may compromise their functional integrity.[1,2]

B) Lipid peroxidation

Lipid peroxidation is another consequence of decreased antioxidant mechanisms with aging. Reaction of ROS in the presence of redox active metals with the double bond of polyunsaturated fatty acids (PUFAs) produces oxidized lipids which may further result in a large number of reactive electrophilic aldehydes including malondialdehyde (MDA), 4-hydroxy-nonenal (4-HNE), 4-oxo-2-nonenal (4-ONE) and acrolein.[7] Lipid peroxidation has been reported to be elevated in the brain with age. MDA was increased in the cytoplasm of neurons and astrocytes in normal aging, but was barely detected in normal young subjects.[8] All of the biologically active aldehydes e.g. acrolein, 4-HNE and 4-ONE are capable of depleting reduced glutathione (GSH), and activating DNA damage and apopotosis in human neuroblastoma cells.[9,10] Amongst the α, β-unsaturated aldehydes, acrolein and 4-HNE have increasingly been implicated in the pathogenesis of AD and PD.[11,12]

C) Oxidative DNA damage

In normal tissues, 10,000 oxidative interactions occur between DNA and endogenously generated free radicals per human cell per day,[13] resulting in damaged nucleotides and strand breaks. These oxidative DNA lesions can block genome replication if not repaired properly. One of the most common lesions is 8-oxo-7, 8-dihydroguanine (8-oxoG); a hydroxyl radical-induced modification of guanine and its level is elevated four times in old brains compared to young brains.[14] Mitochondrial DNA (mtDNA) is more susceptible to oxidative stress than nuclear DNA (nDNA) owing to its close proximity to the ROS generating site and the lack of protective histones combined with a lower capacity for DNA repair. The rate of increase in the 8-oxoG levels was 10 times more in mtDNA than in the nDNA in the cerebral cortex and cerebellum from humans with age.[15] An increase in nuclear and mitochondrial DNA oxidation products have been observed in AD and PD patients.[1,16]

3. The healthy brain during aging: dietary and lifestyle factors

Recently epidemiological studies have also identified dietary factors associated with the decreased risk of AD and PD. Among these, a higher adherence to a Mediterranean diet (MediD) could be associated with slower cognitive decline and reduced risk of AD.[17] Several plant based foods i.e. vegetables, fruits, legumes, cereals and olive along with wine are important components of MediD. These foods are enriched in polyphenols antioxidants that are able to protect neuronal cells in various *in vitro* and *in vivo* models of AD and PD through different intracellular targets.[18] Polyphenols may simultaneously modulate multiple oxidative stress-induced disease-modifying mechanisms involved in AD and PD progression.[18] These findings from epidemiological studies may be further useful in determining the dietary interventions needed for promoting healthy brain aging.

In conclusion, accumulating evidence supports a role of oxidative stress-induced increase in lipid peroxidation, protein oxidation, and DNA damage in the neuronal degeneration and death during aging, AD and PD. Furthermore, there is considerable evidence that dietary antioxidant especially, polyphenols, have neuroprotective effects on preventing or reversing oxidative stress induced -changes of cognitive and motor functions in normal aging, AD and PD and, as such, should be included in intervention strategies for the prevention of AD and PD. ■

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Manjeet Singh

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A young perspective on an aging disease

Eli York

University of British Columbia

In 2012, the World Health Organization announced that dementia affected 35.6 million people worldwide, a number predicted to rise to 81.1 million by 2040, making it a "public health priority."[1] The associated economic burden is over $604 billion US, largely due to costs of long term intensive care.[1] In contrast, there are only five FDA-approved drugs for Alzheimer's disease (AD) treatment, which slow cognitive decline but do not provide a cure.[2] Although there has been a surge of research on AD and related dementias, our understanding of the disease – and potential cures – have not seen satisfactory advances. Why is there such a disparity between amount of research and number of scientific breakthroughs? One possibility is that, until recently, this field has been stuck in a narrow view of AD mechanisms. As is a danger in all disciplines, main ideas potentiate and become the dogma, dictating how researchers design their experiments. In AD research, we see this in its intimate tie to amyloid-β plaques and the use of genetic mouse models. Finally, the past bias is made clear by the promising developments of researchers who have approached AD from fresh angles.

AD was first described in 1906 by Dr. Alois Alzheimer, who characterized it by the presence of neurofibrillary tangles and amyloid-β plaques.[3] To this day, AD is confirmed only at autopsy by the presence of plaques and tangles.[4] Therefore, these features have become a hallmark of AD, and they are the focus of most research aims. From this sprang the amyloid hypothesis of AD, which is rich in scientific literature and which often targets clearance of plaques to treat dementia.[5] In these experiments, amount of amyloid pathology is often used as a marker of treatment efficacy. However, plaques develop normally throughout aging brains, even in healthy individuals with no signs of cognitive impairment.[6] In AD, there is evidence that brain areas with the highest plaque loading do not correlate with degree of neurodegeneration.[4] Even once it was recognized that the $A\beta_{42}$ oligomer is the more toxic form of the protein, research continued to be driven by studies targeting plaques, or that use them as an indicator for degree of dementia.

Another obstacle in AD research is the lack of appropriate animal models. Mutations in genes that increase amyloid-β plaques have become the classic AD mouse model.[7] These mutations were identified in families with high prevalence of AD; however, genetically inherited AD accounts for only 1-5% of total cases, while the majority are sporadic.[8] Since mechanisms causing sporadic AD are unknown, there is no appropriate mouse model to investigate treatment methods. Currently, the only factor clearly associated with sporadic AD is age, and the average mouse lifespan is only two to three years. It is likely that the environment of a two-year-old brain, even with genetic mutations, is very different from that of an 80-year-old brain. These inequalities may explain the abundance of promising therapeutics for mice that do not hold up in clinical trials, as seen recently with Solanezumab (Eli Lily) and Bapineuzumab (Pfeizer/Johnson & Johnson). Therefore, if we hope to treat sporadic AD in human patients, a more appropriate animal model will be needed.

Our knowledge on the roles of amyloid-β plaques and neurofibrillary tangles will no doubt be invaluable to uncovering the secrets of AD. However, focusing too narrowly on one facet of a disease comes at the expense of overlooking critical factors or complex interactions between systems. AD truly develops over a lifetime, so focusing solely on aging-related properties risks missing potential initiators of the disease, as well as opportunities for early intervention. In fact, promising current research incorporates non-genetic risk factors such as lifestyle, traumatic brain injury, and the immune system. One recent paper has analyzed the effects of cellular oxidative stress as a potential risk for sporadic AD.[9] Another group focuses on an excess of pro-inflammatory signaling in AD, and they has developed Etanercept, a TNFα inhibitor.[10] This ▶

drug has reached clinical trials and is showing promising results in tests of cognitive performance, although its exact mechanism of action is not well understood. Clearly, recent unconventional research should be pursued and perhaps combined with other fields to create a multifactorial approach to a complex disease.

It is important to take our vast resource of information and approach the study of diseases from fresh directions to better understand how they can be prevented and cured. The future of scientific discovery is exciting as methods of imaging and analysis are being improved, providing clearer insight into both the process and time-course of disease progression. This discussion of AD underscores the importance of innovative research that challenges dogmas in making scientific advancement possible. This is both our aspiration as researchers and our responsibility as a society.

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Eli York

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Main Submission

A multi-level approach to addressing mental health stigma in Canada

Thilina Bandara

University of Saskatchewan

For the approximately 6.7 million Canadians who experience mental health issues, isolation, social exclusion, and discrimination associated with stigma continue to prevent many from seeking help.[1,2] In 2012, Canada became the last G8 country to draft an official national mental health strategy to improve the lives of those affected by mental illness. According to the Mental Health Commission of Canada's (MHCC) *Changing directions, changing lives: The mental health strategy for Canada*, everyone has a role to play in eliminating stigma against those living with mental health issues.[3] While many anti-stigma campaigns have been piloted across Canada, this new strategy formalizes leadership and promotes the implementation of a national program. With this important step, the opportunity for large-scale advancements in mental health has arrived, including the potential to collectively address stigma.

Stigma and negative stereotypes against those with mental health issues can manifest as discrimination, including denial of employment, limited housing options, and marginalization from professionals towards those with a history of mental health concerns.[4,5] The highly complex nature of this problem requires leadership and coordination. In Canada, former Senator Michael Kirby has demonstrated such leadership through his long-term commitment to reducing stigma against people with mental health diagnoses. By introducing this topic to the senate in 2006, and with his subsequent advocacy work, his goal is to create a national movement against stigma.[6]

Anti-stigma initiatives must be evidence-based and include successful advocacy, targeted interventions, and participatory approaches to research. At the macro level, advocacy can help mitigate stigma-perpetuating behaviors in the media. An example of influential anti-stigma advocacy was the cancellation of the American Broadcasting Corporation's (ABC) television drama, *Wonderland* in 2000. ABC's decision to stop the show has been attributed to heavy backlash from mental health organizations regarding the show's characterization of mental health patients as dangerous and violent. Though unlikely to eradicate individual stigmatizing attitudes, organizational advocacy such as this has the potential to build awareness of stigma across large audiences.[7,8] The recent 'Let's Talk' campaign launched by Bell Canada Telecommunications Corporation was an encouraging step towards further awareness and dialogue at the national level. Designed as a fundraising event, Bell Canada donated 5 cents for each long distance call, text, 'Let's talk' tweet, and Facebook share that occurred on February 14, 2013. Thanks to over 96 million communications, Bell Canada raised over 4.8 million dollars for Canadian mental health programs.[9] Similar efforts must continue to be evaluated for their effectiveness.

Targeted anti-stigma campaigns demand a multi-pronged approached. As Corrigan et al.[7] point out in their meta-analysis of anti-stigma campaigns, there is no one method that will change attitudes associated with mental illness. Their results suggest that mental health educational campaigns are especially effective in adolescent groups, while person-to-person contact with those who have experienced mental health issues has been shown to be beneficial with adults.[7,10] For example, an evaluation of a pilot anti-stigma program that incorporated personal stories from self-advocates who had experienced mental illness demonstrated positive attitude change among health care workers in British Columbia.[11].

Integrating mental health consumers into research is another potential avenue for reducing stigma. The Canadian Mental Health Strategy[3] emphasizes the value of including those affected by mental health issues into the all levels of action, to discuss explicitly what worked for them, what areas are deficient, and where resources are best allocated. For example, the research agenda put forward in the Strategy provides a highly compelling ▶

case for *inclusive* study designs by encouraging the use of both the traditional biomedical approaches – psycho-social, clinical, and neuroscience research, as well methods that incorporate those impacted by mental illness into the creation of knowledge and practices based on lived experience.[3] Framing the national discussion on mental health with people who have experienced or are currently experiencing mental health concerns is another important step towards reducing stigma.

With a renewed sense of direction, Canadians have an opportunity to progress the mental health agenda and alleviate the effects of stigma so that individuals can confidently access recovery services. Taking part in social activism, conducting evidence-based targeted campaigns, and practicing inclusivity in research methods can increase awareness of stigma among those in the field. While the authors of Canada's Mental Health Strategy are quick to admit that their large-scale recommendations to address systemic deficiencies in mental health care will take years to properly implement, helping to reduce stigma is one way we can improve the well-being of all Canadians today. ■

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Main Submission

Growing up with cerebral palsy: What are the concerns for mental health?

Laura Brunton

University of Western Ontario

Cerebral palsy is a movement disorder accompanied by weakness and a myriad of associated secondary conditions including joint deformities, pain and fatigue; and is traditionally regarded as a pediatric neurological disorder.[1] However, the majority of children with cerebral palsy will inevitably become adults with cerebral palsy[3] and transition into a healthcare model with little focus on their specific needs, including mental health concerns. There is large variability in the motor impairments related to cerebral palsy.[2] Related to the wide severity spectrum associated with this condition, individuals with cerebral palsy need varying degrees of support in a number of areas including physical, social, and psychological.

The period between childhood and adult life is particularly important for individuals with cerebral palsy. Adolescence is a trying time for any individual; however, adding a physical disability and the process of learning to self-manage their own healthcare can add further stress.[4] There is a great deal of literature regarding parental stress in caregivers of children with cerebral palsy; yet there is a profound lack of information about the impact of cerebral palsy on the mental health of the child or teen. If parents of these children are feeling the stress of navigating the healthcare needs associated with cerebral palsy, it is not unrealistic to expect a similar impact on the adolescent when first beginning to take responsibility for their own care.

The relationship between lack of participation in meaningful activities and mental health issues, including depression and anxiety, has not yet been explored in adolescents with cerebral palsy specifically. However, children with chronic health conditions are consistently concerned with developing and maintaining friendships, and increased social isolation can have a negative effect on their quality of life.[4] Adolescents with disabilities have the same dreams and aspirations for adult life as all young people;[5] however, they can be restricted in their opportunities to practice or develop the life skills required to achieve specific goals and participate in meaningful activities. Often the lack of available support and resources to develop these skills can lead to further social isolation and withdrawal from community participation.[6] It is unknown if children and adolescents with cerebral palsy experience the same mental health concerns described in other chronic health conditions, or if the specific diagnosis and physical manifestation of cerebral palsy has unique characteristics related to mental health. However, there are increased rates of depression and psychological difficulties experienced by children and adults with cerebral palsy compared to their age-matched peers.[7,8]

The nature of the relationship between common physical symptoms of cerebral palsy and mental health concerns has not yet been clearly described and warrants further study. However, in an ongoing study, several individuals with cerebral palsy have described a reciprocal relationship between stress and fatigue whereby increased stress leads to further exacerbation of physical symptoms and vice versa (Brunton & Bartlett, unpublished data). This relationship needs to be studied directly to understand the impact of mental health issues on the physical symptoms of the condition.

Perrin and colleagues[4] have suggested that the severity of the impairment and the presence of pain can influence or intensify the psychological impact of chronic conditions during adolescence. Chronic pain and fatigue are common physical symptoms of cerebral palsy and may intensify any underlying mental health concerns as individuals with cerebral palsy become adults. In a recent study, van der Slot and colleagues demonstrated a relationship between severity of fatigue and depressive symptoms in adults; however, the strength and impact of this relationship during the adolescent years is still unknown.[8] Similarly, another study has demonstrated significant ▶

moderate correlations between the number of painful sites and mental fatigue in non-ambulatory adults with cerebral palsy.[9] In light of this emerging correlational evidence there is a need for further investigation into the relationships that exist between psychological and physiological symptoms, in addition to understanding the basic psychological impact of living with cerebral palsy.

There is a dearth of information about the mental health concerns of individuals with cerebral palsy across all stages of life. The information available highlights the need to explore the mental health concerns adolescents with cerebral palsy face during late childhood through the transition years and into early adulthood, particularly since adolescence comes with additional stresses (including learning to self-manage their condition and coping with social isolation). Uncertainty and unpredictability experienced by individuals with cerebral palsy may cause increased psychological stress and potentially increase the expression of physical symptoms associated with cerebral palsy. Further information is needed about the health concerns related to depression, anxiety and stress experienced by adolescents with cerebral palsy. Clinicians need more information to assist with strategies and specific intervention planning to help these individuals cope with and anticipate the demands of transitioning to adult life. ■

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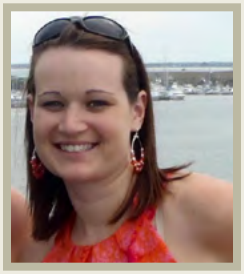

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Laura completed her MSc at Western University under the supervision of Dr. Doreen Bartlett. Her master's research centered on determining the validation, reliability, responsiveness and sensitivity-to-change of two abbreviated versions of the Gross Motor Function Measure (GMFM-66) for children with cerebral palsy. Laura is currently in a combined PhD/Master's of Physical Therapy program at Western University and her current research focus is understanding and measuring fatigue in adolescents and young adults with cerebral palsy.

Main Submission

Using lived experiences to help identify needed mental health services changes

Lorna Corzine

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Over the past several years, mental health care has moved from the sidelines and into the spotlight of health policies throughout Canada. In 2006, a Senate committee prepared an in-depth report on the state of mental health care in Canada and urged a transformation of the country's mental health system to a "community-based, integrated continuum of care."[1] This idea is not new, however, as Ontario's mental health policy has been struggling since 1993 with the notion of creating "a coordinated system with greater emphasis on community-based mental health care."[2] These grand views are to be commended, but it is difficult to quantify and measure any movement toward these goals. While data about the access and use of mental health services provided by hospitals can be easily gathered,[3] the challenge is in collecting data from community-level organizations.[4] There appears to be a lack of standardized reporting structures that follow transitions from hospital-provided services to community services, thereby making analysis of the effectiveness of changes challenging. Likewise, there are few qualitative studies that examine Canadian client experiences within mental health care systems that bridge hospital and community.

As a doctoral student with mental health issues, I recently experienced the mental health care systems in three communities within 150 kilometers of each other simultaneously. Using my own experience as a backdrop for this discussion, I encountered the following realities as I tried to advocate for help during my crisis. The first responder was a small community hospital where my needs were quickly addressed and I was required to speak with a crisis counsellor before being released. I continued to see the counsellor and attended a six-week wellness group session to fill the wait time between intake and availability of a mental health therapist. Once assigned a therapist, I then had access to the visiting psychiatrist. From the moment of my crisis until I released myself from their care, I had continual connections with people who provided me with supportive assistance.

My family physician, in a much larger city, realized my need for immediate psychiatric assistance and made a referral within his community. The centralized intake and referral program put me on a waiting list that was expected to take at least four months. All other programs were similarly waitlisted and no other interventions were immediately available. Frustrated with the wait times to see a psychiatrist, I also searched a smaller city nearby. There was no centralized system for psychiatric or other services and no one I contacted was able to provide alternatives or suggestions of available services.

All three communities were vastly different in their approach to mental health care even though they all fall under the same Local Health Integration Network (LHIN) in Ontario. The mandate of the LHIN is the development of health priorities and strategic directions for their communities and includes increasing access to mental health services.[5] However, Kirby and Keon[1] anticipated this type of variance and noted that services would not be the same between provinces, regions, and even municipalities due to differences in communities. While this would make the creation of one national health care model unwise, they do state it is important to provide a continuum of basic services.[1]

In many regards, I understand that my experiences were not unique. The Senate report[1] contained the voices of many people with mental illness who shared their experiences within the mental health care system in Canada. They noted six-month wait times, lack of information about support, confusion and frustration in accessing services, and even services which were not available.[1] Service providers themselves continue to identify areas that are lacking, such as client input, coordination with service ▶

systems, overall resources, accessibility to treatment, and an absence of collaboration between service providers.[6] Even family physicians are frustrated by wait times for mental health referrals, feedback regarding their clients, and overall knowledge of services available.[7]

However, unlike my experience, many people are only able to access services within their area. It is therefore important to realize that if someone only experiences something in one way, how can he or she know to ask for something different? Further, how can communities know which changes to make to address these unknown gaps? With very few research studies investigating the lived experiences of outpatient and community mental health service clients in Canada, addressing change proves difficult. However, Rudnick et al. remind us that "knowing the lived experience of people who have mental health challenges is considered instructive and hence potentially helpful for… mental health care providers."[8] Utilizing this qualitative approach in and across communities throughout Canada may help identify differences between communities and provide options for change. Only by encouraging clients to identify what works, what does not work, and what they need, can true mental health service reformation begin. ■

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Autoimmune synaptic protein encephalopathy syndromes and the interplay between mental health, neurology and immunology

Gregory S. Day and Harry E. Peery

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Indirect evidence supporting the organic underpinnings of mental illness has accumulated over the past five decades, driven by advances in neuropharmacology, neurochemistry, neuroimaging, and neuropathology, and by expanding knowledge of the structural and ultra-structural changes that occur within the brains of patients with behavioural and affective symptoms.[1] Yet, despite a growing body of evidence, a distinction continues to be drawn between psychological anomalies of the mind and organic disorders of the nervous system. The recent isolation and characterization of pathogenic autoantibodies within the blood and cerebrospinal fluid of patients with symptoms and signs commonly associated with 'mental illness' raises new questions about the origins and pathogenesis of behavioural and affective disorders, providing a timely and welcome challenge to the ideology that divides mental illness and neurological disorders. ▶

ASPES	Antibody Target	Common Clinical Features
Anti-NMDA-receptor encephalitis	NMDA receptor: GluN1/GluN2B subunits	• Psychoses, behavioural/affective symptoms • Encephalopathy • Hyperkinetic movements • Seizures • Central hypoventilation and autonomic instability
Anti-AMPA-receptor encephalitis	AMPA receptor: GluR1/GluR2 subunits	• Psychoses, behavioural/affective symptoms • Encephalopathy
Anti-$GABA_B$-receptor encephalitis	$GABA_B$ receptor	• Psychoses, behavioural/affective symptoms • Encephalopathy • Seizures (early in disease)
Anti-glycine-receptor encephalitis	Glycine receptor	• Psychoses, behavioural/affective symptoms • Encephalopathy
Anti-potassium channel-associated-complex encephalitis	LGI1	• Psychoses, behavioural/affective symptoms • Encephalopathy • Hyponatremia • Seizures (brief tonic-myoclonic seizures)
	Caspr2	• Psychoses, behavioural/affective symptoms • Encephalopathy • Peripheral nerve hyperexcitability (Morvan syndrome)
Anti-GAD encephalitis*	GAD	• Psychoses, behavioural/affective symptoms • Encephalopathy • Seizures • Brainstem dysfunction

Table 1: ASPES defined

Abbreviations: NMDA = N-methyl-D-aspartate; Glu = glutamate; AMPA = α-amino-3-hydroxy-5-methylisoxazole-4-proprionic acid; GABAB = gamma-aminobutyric acid-B; LGI1 = leucine-rich glioma-inactivated 1; Caspr2 = contactin-associated protein-like 2; GAD = glutamate decarboxylase

*The role of anti-GAD antibodies in ASPES requires clarification; unlike other ASPES, anti-GAD antibodies are directed against intracellular antigens and are frequently described in association with other autoantibodies (most notably GABAB)[3]

Autoimmune synaptic protein encephalopathy syndromes (ASPES) encompass a growing group of clinically-recognizable diseases associated with psychiatric symptoms, progressive neurologic dysfunction, and response to immunosuppressant therapies. Expanding work in neuroimmunology has only begun to decipher the relationship between individual syndromes and circulating autoantibodies, allowing syndromes historically defined by the absence of a known etiologic agent (i.e., 'demonic possession,' 'idiopathic encephalitis,' 'limbic encephalitis') to be defined by the presence of a specific pathogenic antibody. To date, a number of receptor-specific autoantibodies have been described in association with ASPES (Table 1).[2,3] Of these, the syndrome associated with autoantibodies against central nervous system N-methyl-D-aspartate (NMDA) receptors remains the most prevalent and best-characterized.

Patients with anti-NMDA-receptor encephalitis (ANMDARE) commonly present with abrupt-onset symptoms including hallucinations, delusions, apathy, fear, depression, memory loss, and confusion/encephalopathy[4-6] – analogous to symptoms reported in healthy adults exposed to the NMDA receptor blocking agent, ketamine.[7] For this reason, patients presenting with ANMDARE are often assessed by psychiatrists and other mental health professionals.[4] Left untreated, increasingly severe symptoms may emerge, including hyperkinetic movement disorders (commonly oral-facial dyskinesias), seizures, and central hypoventilation with autonomic instability.[4-6] Seventy-five percent of patients require admission to intensive care units for cardiorespiratory support.[5] The diagnosis is confirmed by detection of autoantibodies directed against the GluN1- and/or GluN2B-subunits of the ionotropic glutamate-binding NMDA receptor complex using standard indirect immunofluorescence techniques, or more preferably in combination with an adapted cell-based assay using tissue culture cells overexpressing transfected complementary DNA representing the single or assembled GluN1-GluN2-subunits.[2] NMDA receptors are found in highest concentrations within the hippocampi, forebrain, basal ganglia, spinal cord, and cerebellum,[4] mediating a critical role in synaptic plasticity through regulation of intracellular calcium influx. Thus, autoantibody-receptor binding may preferentially affect structures responsible for memory, personality, movement, and respiratory drive, provoking the unique constellation of symptoms and signs that characterizes ANMDARE by inducing receptor internalization and/or cellular apoptosis[4,8]

Much has been written concerning putative disease pathogenesis since the first clinical reports of ANMDARE were published in 2007.[9] Early reports of ovarian teratomas in 59% of cases led to speculation that ANMDARE developed as a consequence of an immune response directed against NMDA receptors expressed on tumour cell surfaces.[9] More recent case series suggest that a tumour is detected in 38% of patients overall;[5] thus, while tumours may go undiagnosed in some patients, additional tissue sites are likely involved in disease pathogenesis. The role of host and environmental factors in triggering and promoting development of autoimmunity is the focus of ongoing research.[2]

Beyond informing our nascent knowledge of disease pathogenesis, expanding clinical experience has increased our understanding of disease prevalence. The accrual of 577 patients by a single research group over a five-year period[5] asserts that ANMDARE is not a rare disease, but rather a rare diagnosis. The diagnosis may be especially rare in patients labelled with 'mental illness.' In a single neuropsychiatric centre, anti-NMDA-receptor autoantibodies were detected in 7.8% (4/51) of patients with a diagnosis of schizophrenia/schizoaffective disorder,[10] emphasizing the importance of considering the diagnosis in all patients with progressive behavioural/affective disturbances without a known etiology.

Appropriate treatment of patients with ANMDARE demands prompt initiation of immunosuppressant therapies. Consensus recommendations derived from case experience support the use of increasingly toxic therapies, beginning with high-dose corticosteroids and/or intravenous immunoglobulins; cyclophosphamide and the anti-CD-20 monoclonal antibody, rituximab, are recommended for those who fail to respond to first-line therapies.[6] With optimal treatment, the prognosis is good: over 75% are alive with minimal or no disability within two years of diagnosis.[5] Delays in treatment or *under*-treatment, however, are associated with longer times to improvement, longer ICU stays, lower chances of recovery, and a higher risk of relapse.[5,6] Mortality is reported in 6% of cases.[5] For these reasons, it is critical to promote early diagnosis and treatment of ANMDARE; it is also critical to ensure that longitudinal care is provided within tertiary care centres with experience in the multidisciplinary management of ASPES.

The discovery of a highly-treatable group of diseases presenting with behavioural/affective symptoms and progressive neurological dysfunction provides a ▶

well-timed opportunity to strengthen clinical and research partnerships between the fields of psychiatry and neurology. Further work considering ASPES will be best performed by clinicians and researchers working together to ensure that patients with 'mental illness' receive appropriate diagnostic investigations and subsequent treatments, leaving the dogma that divides mental illness and neurological disease where it belongs: in the past. ■

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Gregg Day is in his final year of neurology residency at the University of Toronto, and is pursuing post-graduate training in neurodegenerative and antibody-mediated brain diseases. He is a founding member of the Anti-NMDA Receptor Foundation, and serves as the Clinical Director. His research focuses on characterizing the clinical presentation and improving treatment of patients with antibody-mediated brain diseases.

Harry Peery

Harry Peery took the long road to his PhD, working as a critical care nurse before returning to academia. Harry successfully defended his PhD in neuropharmacology in 2013 at the University of Saskatchewan, and is engaged in post-doctoral research at Atomic Energy of Canada, Ltd, through McMaster University. Harry is a founding member of the Anti-NMDA Receptor Foundation, and serves as the Research Director. His research focuses on deciphering the pathogenesis of antibody-mediated brain disease.

Main Submission

Importance of considering methodological variables in rat studies

Namrata Joshi

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Developmental stress exposure is a risk factor for developing a host of neuropsychiatric disorders in the future.[1] Establishing causal links between developmental stress and such disorders necessitates the use of animal models.[1] Although such studies attempt to use similar experimental designs to seek answers to similar questions, they often end up with divergent results. For example, a recent study examining effects of stress on hippocampal neurogenesis failed to replicate the results of a number of earlier studies; it was speculated that subtle differences in animal housing, handling or other methodological factors may have been responsible.[2] Similarly, the effects of amygdalar lesions on activation of the body's main stress response system, the hypothalamic-pituitary-adrenal (HPA) axis, are reported to be divergent; again, the discrepancy was partly explained by factors such as choice of rat strain and animal housing conditions.[3] My own research experiences with stress exposure in adolescent rats demonstrated similar divergence from published findings that can best be explained by subtle methodological differences between studies. This commentary discusses three issues related to animal breeding and rearing that may contribute to variability in outcomes when investigating stress in rats: the diurnal light cycle in the rats' housing environment, features of housing complexity such as cage size and population density, and features of animal transport prior to experimentation.

The first factor is the potential effect of the diurnal light cycle under which the experimental animals are housed. Rats, as nocturnal animals, are most active during their subjective night. Both basal[4] and stress-induced activity of the HPA axis shows diurnal fluctuations. For example, repeated restraint stress induces a greater impact on food intake during the dark phase (night) of the light cycle of rats.[5] Despite the potential for discrepant results, testing rats at different times in their circadian cycle occurs routinely in stress response research. For example, Bourke et al.[6] and Yogarson et al.[7] looked at the social rearing environment and anxiety-like behaviour during different phases of the diurnal cycle.

The second factor is the potential difference in home cage features of the experimental animals; two features are of primary importance. First, home cage dimensions and the number of rats housed in each cage dictate the volume of space available to each animal. These can differ between studies and since overcrowding is a significant stressor[3], too little space can result in all animals, including those serving as controls, becoming stressed, thereby confounding differences between experimental and control groups. Secondly, the number of cage mates available may affect the social interacting, which can impact rat behaviour and physiology, especially in adolescent rats.[6,7] Furthermore, the outcome of a stressor protocol can be affected by the degree of social support available in the form of cage mates.[8] Thus, a seemingly simple decision such as how many animals to house together in a defined space can significantly affect the outcome of the study.

A third factor that may influence results of stress studies is animal transport and/or acclimatization before an experiment. Transport is a complex experience that can includes exposure to a complex array of physical, physiological, and psychological stressors.[9] It is common practice to acclimatize transported animals for one week to ten days before experimental use and ideally, this would be long enough for stress response parameters and other experimental variables to return to a baseline level. Unfortunately, limited information is available on the ideal acclimatization time in rats.[9] It is noteworthy that transportation conditions can even have a generational effect, as transporting pregnant animals can induce prenatal stress. The early environment is likewise important.[10] Specific data on effects of transport ▶

on various rat strains and sexes should be determined. Although sometimes more costly, breeding experimental animals in-house would allow researchers greater control over the pre-natal and early post-natal environments. It is, therefore, worth considering this option in studies that explore questions about the biology of the stress response.

Because the precise effects of each of the described factors is difficult to gauge, and rats can be exposed to multiple factors simultaneously, it is more practical to take these factors into account *before* an experiment begins. To this end, researchers should conduct studies on the effect of these issues on various stress-response parameters. Publication of reviews of the effects of such methodological factors on previously conducted research on stress would also prove to be beneficial. In a climate where funding for research is limited, it is vital that methodological questions be clearly addressed to facilitate replication of results. ■

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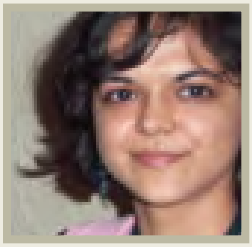

Namrata Joshi

Namrata obtained her undergraduate degree in biology from University of Western Ontario, and her Masters degree from Queen's University. She is currently a Ph.D. candidate in the Department of Medical Neuroanatomy at Dalhousie University. She is interested in the role of environmental factors such as chronic stress during adolescence in the etiology of psychiatric disorders such as schizophrenia, and Major Depression. In her spare time, she hosts a radio show on science called Little Grey Cells at Dalhousie University's local radio station (CKDU).

Main Submission

Huntington's Disease: Advances, controversies, and challenges

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Huntington's disease (HD) is a progressive neurodegenerative disorder with a worldwide prevalence of about 4-7 per 100,000.[1] In 2011, there were approximately 639 people diagnosed with HD in Canadian long-term care facilities alone.[2] HD is characterized by progressive motor dysfunction, cognitive impairment, and psychiatric disturbances.[1] Motor abnormalities can manifest with chorea, bradykinesia, and apraxia, and later progress to dystonia.[3] Cognitive impairment involves difficulties with executive functioning, as well as visual and attention deficits, while psychiatric symptoms can lead to aggression and depression.[3] HD normally appears between the ages of 30 and 45 with variability in onset and severity of symptoms.[3] It is caused by a CAG triplet repeat expansion in the *huntingtin* (HTT) gene located on the short arm of chromosome,[4] producing a mutant protein responsible for CNS degeneration.[4,5] More than 40 repeats of CAG is associated with occurrence of the disease by age 65, with longer CAG repeats predicting earlier onset.[5] A juvenile form of HD also exists that can occur as early as five years of age.[1]

There are many standard pharmacological medications available for the treatment of psychiatric symptoms, and motor dysfunction can be alleviated with tetrabenazine and antipsychotic drugs.[3,4] However, no well known treatments have been found to greatly improve cognitive impairment.[3] To date, psychotherapy, speech therapy, and physical and occupational therapy are the most effective treatment methods available.[6] Advances are being made through stem cell research to replace lost neurons as a form of late-stage intervention, making it possible to regain some loss of function.[5] Evidence also suggests that coenzyme Q10 and daily doses of creatine may improve the functional decline in HD patients; Phase III studies are under way to assess these effects.[3] Neuroprotective strategies are being examined to help delay the progression of HD while the use of disease modification biomarkers can recognize HD development before disease onset.[7] In the future, scientists are looking towards enhancing clearance of mutant HTT, improving transcriptional deregulation, preventing production of the toxic N-terminal of mutant HTT, and switching off expression of the gene itself.[4]

Although we continue to make advances in HD, certain controversies still exist. HD is an autosomal-dominant disease; therefore, bearing children becomes a difficult choice for known carriers. Parents may opt for prenatal screening, however pretest counselling is needed to acknowledge the possibility of pregnancy termination.[4] Direct prenatal screening will reveal the HD gene carrier's status, so linkage analysis may be preferred to maintain status anonymity while using the grandparent's DNA to determine HD risk in the child.[8] Controversy exists around pregnancy termination, not only because many perceive it as the taking of a human life, but the child may not manifest the disease for decades with a possibility of no disease development.[8] Conversely, non-engagement in screening can be interpreted as immoral and irresponsible.[9] Undergoing genetic testing can cause unnecessary stress and significant reduction of "healthy time" with no cure for the disease. Those with HD can also be discriminated against by employers and insurance companies. Although The Canadian Charter of Rights and Freedoms and The Canadian Human Rights Act attempt to prohibit discriminatory practices under enumerated grounds, it continues to be a highly sensitive topic that gives rise to ethical issues of eugenics and genetic discrimination.[10]

Challenges also arise when searching for a cure. For example, making the HD gene inoperative may be a complicated procedure as the gene involved also serves other vital brain functions.[7] The research required to find remedies for HD are impeded by the fact that they require a massive acceleration of a biological process that takes ▶

many decades to develop in humans. It is difficult to find animal models that mimic the progression of the disease in humans. Being a carrier of HD also introduces personal challenges: patients must find new ways to cope with the disorder, both mentally and physically. Their quality of life decreases in conjunction with an increased dependency on others, and there is a negative stigma related to HD that not only affects the patient but also places a burden on those who are closely related. Most importantly, the decisions in life that once seemed fulfilling and simple are now a cause for great concern.

HD sparks the scientific minds of today and emphasizes the ethical issues surrounding life and death. There is a fine balance between what is considered right and wrong while the options available to those with HD are not as straight forward as one may think. It is a debilitating illness that affects all aspects of the individual's life and their decisions moving forward. Many challenges and controversies exist, however experimental research and medical advances are continually being discovered to manage and treat HD. The future seems especially optimistic for a pharmacological breakthrough within this field. Although HD is a difficult illness to endure, in time it may be conquered. ■

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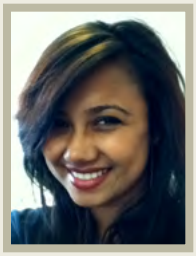

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Main Submission

Keeping pace with social media technology: Implications for the mental health of individuals with neurological conditions

Kelly Ravenek and Mike Ravenek

University of Western Ontario

The ever-changing face of technology makes it difficult for anyone to keep up with the latest and greatest offered to consumers.With advances in social media, the means by which people can communicate with others electronically has grown exponentially in the last decade. Wikipedia, Twitter, YouTube, Skype, Google+ and Facebook are now household names. This has important implications for those living with chronic illness, given that many health consumers actively seek information, advice and support one another via online venues.[1] In fact, numerous support organizations for individuals with neurological conditions now have their own Twitter, YouTube and Facebook pages. Patient groups, such as those in Canada with multiple sclerosis, have already provided a concrete example of how social media technologies can be used to influence research priorities and how research findings should be disseminated.[2] So, what impact can these technologies have on mental health? To begin to address this question, we will draw on examples and reflections from our current doctoral research programs.

Parkinson's disease (PD) and spinal cord injury (SCI) are divergent in their pathology and prognosis, one being a progressive neurological condition with no known cause (in its idiopathic form) and one being an acquired injury. Both, however, can happen to the young or the old, impose functional limitations and have associated mental health concerns. In terms of mental health concerns, depression, stress and isolation are among the most frequently encountered, especially among young adults with PD and SCI.[3-6]

K. Ravenekand colleagues at Parkwood Hospital in London, Ontario are currently using video conferencing and gaming technology to remove barriers to exercise for individuals with SCI. Exercise has a number of benefits for those with SCI, including decreased depression, pain and stress.[7,8] In K. Ravenek's research, video conferencing technology is being used not only to deliver a real-time seated aerobic exercise program but also to deliver exercise counselling while avoiding transportation and environmental barriers. As stated by one participant, "I live in a small community and I know there are not a lot of resources for me; most of the classes I go to now are 20-30 minutesaway, so doing this in my home is fantastic … the people are great and it's fun".[9] As alluded to by this participant, in addition to the benefits of exercise this technology allows for an interactive and social experience both with a trained instructor and peers.

The social benefits of technology have also been observed in M. Ravenek's research which investigates the diagnosis experiences and information needs of young adults with PD. More specifically, M. Ravenek is using a private online-discussion board and YouTube Channel as adjuncts to other forms of data collection. With both of these technologies, participants are able to anonymously and asynchronously (i.e., available 24 hours per day) interact with one another and continue to provide input on the developing results of the project. However, participants have also started to use the discussion board as a means of providing informal support and encouragement to one another. Although measuring depression, stress and isolation was not a focus of this study, participants have provided anecdotal support to warrant a closer examination of the impact of social media on these health issues. Some evidence to suggest that homogeneous PD support groups can improve symptoms of depression has already been reported by Lieberman et al.[10]

Implementation of any new or existing technology warrants many considerations. Participant training is key to promote engagement and to retain interest in the technology being used. Training must also incorporate the 'lingo' associated with the various social media technologies (e.g., friending, threads, tweeting, etc.). Privacy issues must also be addressed. The video conferencing intervention and discussion board, that are part of our research ▶

programs, allow participants to choose an anonymous username. It is also important to comment on the role of monitoring and moderating. The video conferencing technology incorporates in-home monitors as a safety mechanism during all exercise classes. The discussion board is moderated on a regular basis to respond and expand on posts as well as to ensure that appropriate content is submitted.

Social media technologies are, for all intents and purposes, a relatively low-cost option to allow people with neurological conditions to communicate with and support one another. Online support groups and video conferencing are only the tip of the proverbial social media iceberg, and future work should investigate what services individuals are using, how they are using them, and why they are using them. In addition to these contextual questions, there is also a need for evaluation of their effectiveness.[1] It is, therefore, not a question of whether people with neurological conditions are using social media technologies, but how we may incorporate these technologies into our research to evaluate their impact and benefit to those living with a neurological condition. ■

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Main Submission

Psychogenic paralysis: A neuroanatomical explanation of conversion

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Patients who enter a neurological clinic presenting with extreme, unexplained motor weakness or paralysis without any other observable neurophysiological deficits are often diagnosed with a rarely discussed disorder: psychogenic paralysis.[1] This disorder is extremely debilitating, poorly understood,[2] and treatment options are currently limited.[3] Recently Hallett[3] discussed the disturbing reality of the situation. Not only are there an increased number of patients presenting with these unexplained symptoms (5 per 100,000 people, with an average age of 30)[1] but physicians are currently unclear how to treat them. Furthermore, the prognosis for these patients is extremely negative.[3] Shifting our perspective and providing a multidisciplinary approach may be necessary for developing new treatments and improving patient care.

Although Freud referred to psychogenic paralysis as a "conversion disorder", he was among the first to suggest an explanation for these patients' symptoms.[1] He proposed these unexplained motor symptoms were a result of internal mental conflict, and that the expression of the symptoms helped to partially resolve this internal conflict, termed primary gain.[1] Furthermore, the expression of the symptoms rewards the individual with a "sick" status, and offers them benefits such as increased attention or time away from employment, termed secondary gain.[1] Therefore, the patient's internal emotional conflict may be altering their motor function while motivating them to seek any benefits that may be associated with their disability. Although Freud may be partially correct in his theory, it does not provide a framework to begin understanding the underlying neurophysiological mechanisms. Thus, a movement to bridge psychodynamics and neurophysiology is crucial to furthering our understanding of psychogenic paralysis and to improve the prognosis for these patients .[4,5]

With advancements in imaging techniques, specifically functional magnetic resonance imaging (fMRI), we may be able to begin approaching psychogenic paralysis from a more neurophysiological point of view.[3] fMRI studies reveal that psychogenic paralysis patients consistently show drastic over-activation of the amygdala and associated limbic regions,[6] coupled with an inhibition of sensorimotor areas.[7] These limbic regions, and more specifically, the amygdala, have been implicated in a variety of emotional and motivational functions;[8] thus, these results suggest emotional areas of the brain may be responsible for the inhibition of motor areas, resulting in motor weakness or paralysis. Exploring the neuroanatomy of these regions reveals that they are heavily connected through parallel basal ganglia circuits and common mediation points such as the thalamus[9] and frontal lobes.[6] Therefore, it is highly likely that the limbic areas and motor areas modulate each other through their common structures. Researchers have begun applying this knowledge to treatment techniques by seeking to enhance activation levels in motor areas using brain stimulation.[1] Patients appeared to show improvements in motor abilities; however, more work is needed to rule out alternative explanations.[1]

fMRI data and an understanding of the underlying neuroanatomy provide a neurophysiological mechanism by which patients may be experiencing motor weakness. However, as important as these findings are, they do not discount Freud's original interpretation of psychogenic paralysis. Freud was convinced internal conflict ultimately led to the appearance of motor deficit.[1] Based on our current understanding of psychogenic paralysis, Freud may not have been so wrong. A dramatic internal conflict would undoubtedly result in increased amygdala function. The real question is: if the conflict is so severe, can ▶

this over-activation become so great as to shut down, or inhibit, other areas of the brain? Based on current theories of psychogenic paralysis, and fMRI evidence, the answer may be yes.

The bridge between psychodynamics and neurophysiology does not stop there. Freud's second postulate about psychogenic paralysis was that it provides the patient with secondary gain.[1] One might characterize secondary gain as a covert motivation. Through further inspection of neuroanatomical connections one can observe that the amygdala is strongly connected to motivational centres, such as the nucleus accumbens, through the limbic channel of the basal ganglia circuit.[10] Therefore, there may be a neurophysiological explanation to Freud's secondary gain concept.

Original theories surrounding psychogenic paralysis may indeed line up with neurophysiological evidence. Thus, when patients suffering from these disorders seek physicians, a multidisciplinary approach is crucial. Not only should a psychiatrist be involved to begin dealing with the underlying emotional state and its affective result, a neurologist should also be sought to examine the neurophysiological substrate of the patients' paralysis. Furthermore, as psychodynamics may provide us a more complete understanding of what the patient is experiencing, the expertise of a psychologist may also be warranted.

The junction of psychodynamics and neurophysiology is crucial for a well-rounded understanding of how psychogenic paralysis affects patients. Appreciating the neurophysiology behind Freud's primary and secondary gain concepts will give physicians better insight into the patient's psychiatric state. Only through appreciating the patient as a whole and bridging these different medical disciplines can we unlock the mysteries of these harrowing disorders. ■

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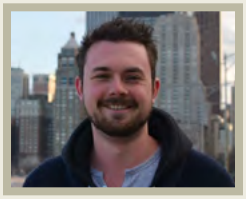

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Main Submission

A knowledge translation perspective on executive function in clinical practice to mitigate chronic pain

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McMaster University

Executive Function

Executive Function (EF) is considered the controlling mechanism of cognition dynamics;[1] where the term "cognition" refers to all neural processes by which sensory information is transformed, modulated (reduced or elaborated), preserved (stored or recovered), and used.[2] To realize the biological process of cognition, we have to consider the information process in neural networks beyond the individual neuron.[3] EF acts as a dynamic part of cognition in the conscious control of thought. From an evolutionary biology perspective, EF is an adaptive response and plays a major role in self-directed sensory-motor action.[4] One may think of it as a collection of interrelated processes that control and regulate thought and action, and that are capable of suppressing habitual responses. EF enables the ability to attend selectively to a stimulus and to inhibit the distraction of other stimuli. A combined analysis demonstrated that the lateral prefrontal cortex (LPFC) cascades EF from premotor to anterior PFC acting as a controlling mechanism depending on the stimuli, context, and episode.[5] The PFC neurons work as part of an integrative network of EF and control cognition with the optimum motor response (Figure 1).
A confirmatory factor analysis study[1] suggested a taxonomy of EF comprised of three moderately correlated, but separable, facets: *shifting* (task switching), *updating* (working memory), and *inhibition* (behavioral inhibition).

EF is conceptualized[1] as the capability of action selection in relation to internal goals organized by the Prefrontal Cortex (PFC). The PFC is functionally important for the temporal integration of sensory information (via the multimodal sensory cortex) in the sequence of optimum behaviour according to the internal goal.[3,6,7] In the PFC, EF operates through dynamic cross-modal association with a temporal organization of behaviour according to the transferred information, like a perception-action cycle.[7] In that cycle, the multimodal sensory association area is integrating sensory information towards movement planning and thinking as an anatomical substrate of higher brain function (e.g. conscious thought, perception, and goal-directed action).[3] The PFC is the highest level of the physiological cortical hierarchy and assumes the prime role for representation and execution of actions.[7] To sum up, cognitive control (i.e. EF) is accomplished by framing of temporal action and by the selection of events, in other words contextual versus episodic control of communication (Figure 1).

Potential Role of EF in Mitigate Chronic Pain

In view of pain neurophysiology, subjective interpretation of pain message goes to three specialized regions of the brain: 1) The Somatosensory Cortex (physical sensation region), 2) The Limbic System (emotional feeling region), and 3) The Frontal Cortex (the thinking or cognitive ▶

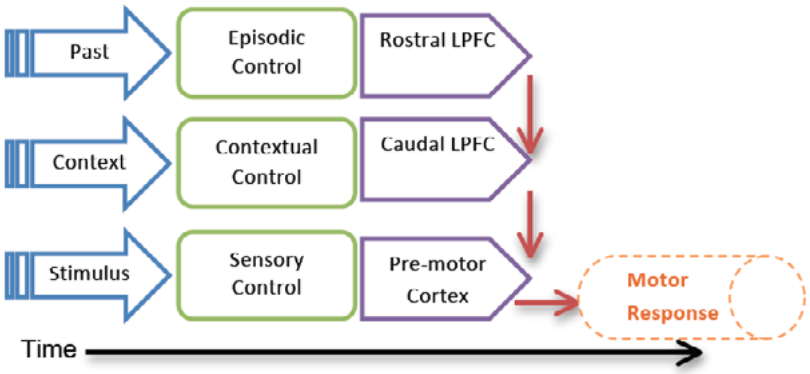

Figure 1: Temporal functional cognitive control processing model (adapted from Koechlin E, et al. 2003, 2007).[5,6] LPFC = Lateral Prefrontal Cortex.

region). The frontal cortex is considered the most responsible area for pain generation, maintenance, integration, and control. More specifically, the PFC is considered as a key source of pain modulation.[8] Evidence suggests that the PFC actively reorganizes after chronic exposure to pain.[9,10] Brain imaging studies demonstrated parallel activation in areas of the brain for EF and the experience of chronic pain. Also, people with chronic pain suffer from poor executive ability[11,12] presumably because they do not have sufficient access to EF to mitigate their chronic pain experiences. Therefore, rehabilitation strategies should aim to improve EF by targeting the areas of the brain that share function with chronic pain.

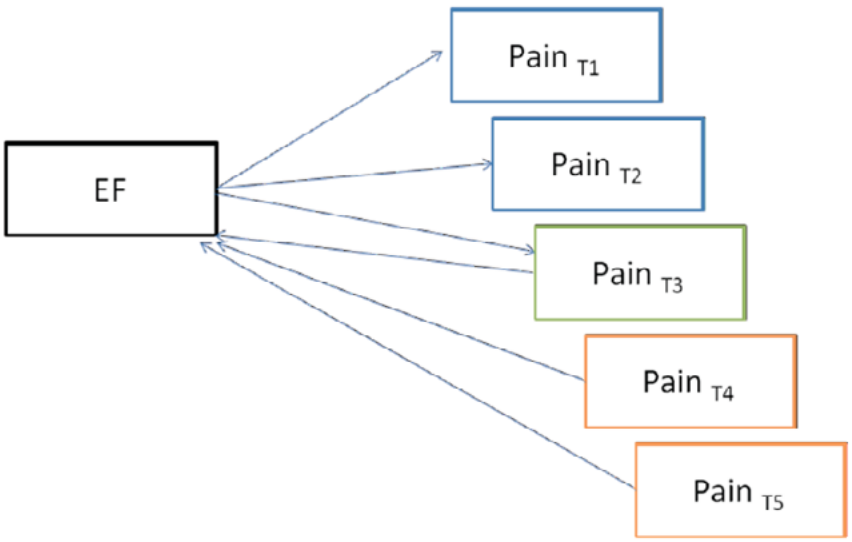

Figure 2: A reciprocal dynamic relationship between EF and Pain,[15] where both are engaged in the overlapping function and capacity-limited cognitive resources over the time (T1 and T2 = acute stage, T3 = transition stage, T4 and T5 = chronic stage). In the chronic stage, pain is inversely related to executive function.[11,12]

The top-down pain modulation (pain inhibitory mechanism) is maintained by a cognitive control mechanism,[13] either by integrating homeostatic regulation or autonomic premotor area activation. Rationally, the faulty top-down control is considered to explain the development of chronic pain.[14] Within top-down cognitive control, pain and EF (i.e. cognitive control mechanism) can be seen as an interlinked dynamic phenomenon in different stages of the pain process, especially in the acute to chronic stage (Figure 2). The pain flare-up condition might further sensitize the nervous system. Appropriate use of EF interventions might help to desensitize the system through the operant conditioning (active behaviour) mechanisms.

Movement and function limitations are common in chronic pain, and it is linked with pain related disability. EF linking strategy (e.g. pacing and graded exposure) might be helpful to reduce pain related disability by maximizing movement and function. Therefore, treatment approaches focusing on cognition improvement (e.g. graded motor imagery, goal setting, altering visual input, graded exposure, tone-pitch recognition, sensory discrimination training programmes, desensitization approach, and sensory-motor interaction targeted exercise) might improve EF and as well as the movement pattern in chronic pain.

Conclusion

Applying EF to the management of pain in a clinical setting can enact a potential source of pain modulation.[8] The conscious control of thought and action are fundamental to motor rehabilitation in chronic pain. Because of the manipulating power in cross-temporal contingencies, EF is important in healthy behaviour practice as well as in the clinical practice of pain management. Further research and effective knowledge translation are essential in this area of research and practice. ■

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Main Submission

Light at the end of the tunnel: A focus on outcomes in mental health services

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Nearly 1 in 4 people will suffer from a mental disorder in a given year – an estimate that has remained consistent over recent decades.[1] Despite this constant incidence, the rate of treatment appears to be increasing.[2] With the provision of more treatment for mental disorders comes along concerns regarding the quality and outcomes attained through such interventions. As part of a national public health strategy aimed at improving mental health, the Canadian Psychiatric Association (CPA) has issued recommendations to use evidence-based treatments to reduce distress and impairment and to monitor outcomes.[3] Although an emphasis on promoting evidence-based practice is warranted, it is important to consider that such implementation cannot guarantee the eradication of mental disorders. Even though many process measures exist in mental health aimed at ensuring quality in the delivery of services, the majority have not been shown to be related to treatment outcomes.[4] As such, it is entirely possible that efforts being put forth to recognize and treat mental disorders may not ultimately lead towards improved mental health outcomes.

Factors that may undermine improvements in mental disorders include the current lack of rigorous outcome measurement and frequent monitoring in real-world practices.[3] For instance, the inability to follow-up and measure treatment effects over time could result in the failure to detect residual symptoms, recurrences, as well as adverse effects – all important aspects which could influence clinical decision-making towards an alternate and perhaps more appropriate course of treatment. Thus, part of an early intervention strategy for managing mental disorders should include the early identification and management of recurrences of symptoms or adverse effects which may impede reaching the end goal of therapy. Theoretically, the measurement of outcomes in mental health services is in part contingent on the ability to identify goals of treatment and accurately measure well-defined therapeutic outcomes.[5] This then begs an important question: what is the goal of treatment in mental health?

One definition of a treatment goal might be to achieve a state of remission from a mental disorder, whereby patients no longer experience daily impairments. Various disorder-specific definitions of remission exist based on different thresholds of improvement, which can be summarized in three levels: 1) symptomatic, 2) syndromal, and 3) functional remission.[6] For instance, with bipolar disorder, symptomatic remission invokes a loss of partial diagnostic status when the patient has minimal or no symptoms according to measures such as the Young Mania Rating Scale, Hamilton Rating Scale for Depression (HAM-D), or the Scale for the Assessment of Positive Symptoms (SAPS). Syndromal remission may occur when a patient no longer meets the full diagnostic criteria according to the DSM-IV. Concurrently, functional remission can be achieved when a patient has made a functional (full) recovery to pre-morbid levels after 6-12 months, with a quality of life that is acceptable to the patient. Therefore, some definitions of remission as the end goal of treatment have been established and are based on the use of validated instruments for measuring outcomes and engagement by patients in defining their own goals of treatment. Despite this, the extent to which real-world practices are measuring treatment outcomes has not been well-documented. Additionally, a lack of a recommended treatment monitoring schedule may be further hindering efforts to measure remission or recurrences of symptoms over time.

On the other hand, a barrier to the measurement of outcomes may be that clinicians are limited in the time they have to thoroughly follow-up with their patients for mental health difficulties. This may be particularly true for primary care physicians who frequently care for patients with mental health difficulties. For instance, one study ▶

revealed that primary care physicians spend only an average of 10.7 minutes face-to-face with their patients.[7] This does not appear to leave physicians with much time to assess mental health patients for residual symptoms, recurrences, or adverse effects, let alone attend to other medical concerns. Considering the existing workload placed on primary care physicians, it is not surprising that they often experience a lack of time in consultations with patients suffering from mental health difficulties.[8] Therefore, one of the challenges in following-up on mental illness is the perceived threat of increased demand for health services.

When debating the issue of measuring outcomes, it is important to consider that undiagnosed or untreated mental disorders contribute to a tremendous degree of suffering to patients and a financial drain to society due to disability, lost work days, and excessive healthcare use.[9] It is for these reasons that further research is needed to identify strategies or tools that may assist with the measurement of outcomes. At the same time, it is imperative that healthcare professionals be more vigilant in monitoring patients and more aggressive in pursuing better treatment outcomes for millions of individuals suffering from mental disorders worldwide. ■

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Main Submission

Not so liberating after all: Multiple Sclerosis disease and treatments

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Myelination of neuronal axons is essential for both the normal and rapid electrical conduction along an axon. Multiple Sclerosis (MS) is an autoimmune disorder characterized by the gradual loss of the myelin sheath, eventually resulting in loss of neuronal control. Immune cells typically have limited access to the CNS, but in MS, these cells are able to target myelin and cause inflammation, demyelination of axons and subsequent neurological impairment.[1] Initial onset of MS involves oscillations between remission and relapse, progressing to its chronic state with irreversible damage and permanent disability. In remission, for unknown reasons, the activity of the immune system decreases and the demyelinated axons are remyelinated by endogenous pools of stem cells.[1] As MS progresses into the chronic form, remyelination no longer occurs and the neuronal damage continues to accumulate, eventually leading to paralysis and death.[2]

While the cause(s) of the autoimmune reactivity to myelin is still unknown, it has been linked to genetic and environmental factors. For example, MS is more common in higher latitudes, possibly because of vitamin D deficiency.[3] Due to the complexity of MS, current treatments tend to target specific aspects of the pathology – such as inflammation or remyelination – as opposed to prevention or reversal of the autoimmune response. Most current drug treatments modulate immune system activity, which aim to prevent new lesions and limit further demyelination.[1] Ironically, suppression of the immune system as the only form of treatment may actually be detrimental. For example, inflammation and the subsequent activity of macrophages and microglia are needed to clean up cellular debris. They also release signals important to the initiation of remyelination, therefore playing an important role in remission.[4] In chronic MS, immune suppression therapy does nothing to reverse myelin loss or protect demyelinated axons from further damage.[4] Thus there is much interest in the use of stem cell therapy to reverse the loss of this tissue and re-myelinate naked axons.

A recent controversy is the suggestion by Dr. Paolo Zamboni that MS is caused by the inhibition of drainage from the brain, termed "chronic cerebrospinal venous insufficiency."[5] Dr. Zamboni suggests that MS patients have insufficient drainage of blood from the CNS, causing a reflux action that moves blood back into the CNS via secondary blood vessels. This model further proposes that due to pressure build-up in these blood vessels, there is a resulting leakage of blood into the surrounding tissue that causes a build-up of iron and initiates the immune system's reactivity to myelin.[5]

In chronic cerebrospinal venous insufficiency (CCSVI) treatment – commonly known as liberation therapy – veins are expanded to increase blood flow away from the CNS, which is similar to the mechanism of arterial stent therapy. However, there are a several flaws to this model. CCSVI is a symptom that is often seen in men, yet MS tends to occur primarily in women.[6] There is also a lack of correlation between CCSVI and MS, where not all MS patients have CCSVI, and vice versa.[7,8] Furthermore, it is unclear as to how liberation therapy, or an increase in CNS blood drainage, can inhibit the immune system's sensitivity to myelin. Typically, once the immune system has been activated, as long as the antigen (in this case myelin) is present, the immune system will be active until levels of the antigen have decreased significantly.[9] Lastly, there is no known mechanism by which liberation therapy can result in the remyelination of the damaged CNS. Because of the media attention brought on by the idea of CCSVI, there was a significant push for clinical studies looking at liberation therapy. Clinical studies have begun in several countries, and initial results have been mixed.[7,8] However, with our current understanding of MS pathology and CCSVI, there is no clear evidence or physiological mechanism to ▶

suggest that the benefits of liberation therapy outweigh any of the significant associated risks. These risks include stent migration, blood clots within the brain and subsequently stroke.[8,10]

Despite public focus on liberation therapy as a potential cure for MS, mounting evidence suggests that CCSVI is not correlated with MS, and is unlikely to be effective as a form of treatment.[7,8] Given that immune suppressant therapies can potentially be harmful, current and future research on MS treatment should focus on cell-based therapies, in conjunction with immune modulation to reverse the effects of MS. It is hoped that with a better understanding of the immune system and its activity in the CNS, MS can be detected and prevented. ■

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