camh
FOUNDATION

Impact Report

The Krembil Centre for Neuroinformatics

Powering Data to Empower People

Presented to:

The Krembil Foundation

2023

A Message from CAMH Foundation

Dear Bob, Mark, Riley and members of the Krembil Foundation team:

Thank you for your continued visionary support of the Krembil Centre for Neuroinformatics. You have helped to build the foremost data-driven mental health research centre in Canada, and you are impacting the care we offer people today and the future of care for people living with mental illness around the world.

The public's response to our groundbreaking $500-million No One Left Behind campaign has been tremendous, and each day we make great strides towards our ambitious goal. This would not have been possible without visionary partners like you. We are thankful for your leadership and stand on the shoulders of what we have already accomplished together. We were thrilled to publicly launch a new marketing campaign focused on addiction, which will build on our momentum and spur important conversations about an issue that touches many of our lives.

As you know, the campaign will support the construction of a new Research & Discovery Centre that will consolidate a majority of CAMH's scientists under one roof together with our Krembil team. This will bring cutting-edge research facilities in close proximity to clinical care services, in a building designed with accessibility front of mind. The new Research & Discovery Centre will ensure that more patients and their families can participate in research design and execution, achieving outcomes that are tailored to best meet their needs.

Your latest contribution to the campaign of $25 million will help establish a new home for KCNI in the Research & Discovery Centre. Co-locating the Krembil Centre with other leading CAMH research centres will open the doors to new collaborations for our scientists and give them access to high-quality patient data to transform mental health. Our state-of-the-art laboratories will attract the world's top talent and collaborators to CAMH, who will be supported by chairs, fellowships and discovery funds to drive forward innovations in care.

In its new home, the Krembil Centre will become greater than the sum of its parts. Together, we will accomplish so much more in this incredible new space that will become a symbol of hope for people around the word.

Your philanthropic leadership continues to inspire others, including our corporate partners, like BMO, whose $5 million gift we recently celebrated. Your family is ensuring that the future of mental health research is brighter than ever, giving hope to people living with mental illness today, and ensuring no one is left behind. We can't wait to see what's next.

Sincerely,

Deborah Gillis

Deborah Gillis
President & CEO, CAMH Foundation

A Message from David Rotenberg

Thank you for your generous funding of the Krembil Centre for Neuroinformatics at CAMH. Your continued support has been integral to advancing data-driven innovations in the diagnosis and treatment of serious mental illnesses. The Krembil Centre is a major centre of discovery, an incubator for the careers of promising scientists and a magnet for researchers from around the world eager to collaborate to drive discovery. It's an honour to update you on our progress.

With your support, we continue to grow and expand our KCNI team. In April we welcomed the Digital Mental Health Lab, led by Dr. Gillian Strudwick, Chief Clinical Informatics Officer at CAMH, to the Centre. Her lab's expertise in applied research—bringing innovations from the lab, to the clinic, to the community—will bolster our ability to expedite discoveries into care. The Digital Mental Health Lab shares our passion for creating a learning health system model, where health data and patient outcomes inform and improve patient care using digital tools like patient portals and dashboards. We are thrilled to welcome Gillian, who has deep CAMH institutional knowledge, to the team.

A significant focus of our work this past year has been expanding the reach of the KCNI and leading pan-Canadian data initiatives benefitting people across the country. The BrainCanada Canadian Youth Mental Health Insight (CYMHI) platform, which launched last fall, continues to gain momentum as we recruit for key roles and the procurement process for the underlying data fabric is finalized. In addition, we are expanding our scope to facilitate services provided outside our walls including leading the data and analytics implementation of 9-8-8, Canada's new suicide prevention line launching in November. We are also developing the data platform for the Hub in Cardio-Neuro-Mind Research, based at the University of Ottawa, set to uncover linkages between brain and heart diseases, which impact over six million Canadians.

In this report there are many great stories from our scientist teams who are growing translational impact through their groundbreaking research and offering unique education and development programming. The opportunity to collaborate and learn with them draws the brightest minds from around the world to advance the latest breakthroughs in data-driven mental health research. This is a clear demonstration of the strength of our individual successes, but also the power of our collaborative effort at the Krembil Centre.

Finally, as you know, Sean Hill has accepted a new role in Switzerland into which he will transition over the coming year. We deeply appreciate his leadership over the past six years and wish him well. Sean asked to share this note of gratitude with your family:

> *I want to thank you for the tremendous opportunity you offered me to lead the Krembil Centre. I am immensely proud of what we have achieved together over the past five years, and I am excited for what this team will accomplish in the years to come, fueled by your most recent generous gift. We have begun the international search for my replacement and will ensure a smooth transition, keeping you informed along the way. Thank you.*

Thank you for your continued visionary support of our work.

Sincerely,

David Rotenberg

David Rotenberg
Operations Director,
Krembil Centre for Neuroinformatics

YOUR IMPACT BY THE NUMBERS

105 Total Team Members Including **+27** new team members

61 Trainees Including **+9** new trainees

8 Trainees Graduated

84 Events/Conference Speaking Engagements

113 Publications **+10** increase from 2022

53 Grants Awarded

$9,943,000 Grants Awarded Revenue (KCNI)

Speakers and panel participants at the announcement of BMO's visionary $5 million gift in support of independent research at the Krembil Centre for Neuroinformatics (KCNI) and the future Research & Discovery Centre, from left to right: Deborah Gillis, President & CEO, CAMH Foundation; Sharon Haward-Laird, Group Head & General Counsel and Executive Champion of Diversity, Equity and Inclusion, BMO; Sarah Downey, President & CEO, CAMH; Angie Elliott, Mental Health Advocate and Former CAMH Patient; David Rotenberg, Operations Director, KCNI; Dr. Laura Sikstrom, Project Scientist, KCNI; and Dr. Aristotle Voineskos, Vice President of Research, CAMH.

KREMBIL CENTRE FOR NEUROINFORMATICS HIGHLIGHTS

Digital Mental Health Lab Joins Krembil Centre

As the need for mental health services continues to rise, the opportunity to utilize digital technologies to support care has never been greater. In April, the Digital Mental Health Lab, led by Dr. Gillian Strudwick, a Senior Scientist and Chief Clinical Informatics Officer at CAMH, officially joined the Krembil Centre for Neuroinformatics. The Digital Mental Health Lab works with patients, health professionals and caregivers to ensure that digital mental health innovations are best utilized to benefit those who need them the most. To achieve this, they use implementation science and knowledge translation methods to ensure seamless integration of innovations into routine practice.

As an applied research lab, the Digital Mental Health Lab was brought into KCNI to support bringing the research of KCNI scientists closer to the "clinic" and supporting an applied aspect to other scientists' work (i.e., Why does this important research matter for patients? Families? Clinicians?). The team has already begun collaborating with KCNI scientists including Drs. Marta Maslej and Laura Sikstrom.

A Growing Role at CAMH

After completing her PhD at Univeristy of Toronto (UofT), Dr. Strudwick transitioned from an Advanced Practice Nurse role to a project scientist role with the Information Management Group (IMG) team at CAMH. In this position her research focused on informatics and implementation science, but as her research program grew and evolved, so did her team. In 2018, when she transitioned into an independent scientist role, she formally established the Digital Mental Health Lab in 2018. The lab was the first of its kind at CAMH, focused on the intersections of mental health, implementation science and digital health.

Today, the lab encompasses a diverse team of 17 nurses, researchers and trainees, each with varying backgrounds in health informatics, health administration and health design. The team has published over 100 articles, been part of the COVID-19 provincial science table, presented hundreds of times on their work around the world, won numerous national and international awards and has carved out a path for digital health researchers in the mental health space with an applied focus.

The Future of Digital Mental Health

The future for digital mental health or digital health more broadly is one in which an integrated system exists. Integrating digital mental health tools into care settings and processes is the next step in order to ensure meaningful use and adoption of these interventions. Novel approaches to doing so include the implementation of roles such as "Digital Navigators." The role of a digital navigator in clinical care settings is to provide guidance, support and education to patients and health professionals, in adopting and leveraging digital health solutions effectively.

Learning health systems is a growing trend, where health data and patient outcomes can be used to inform and improve patient care at a given organization. This can be facilitated through the use of digital health tools such as patient portals and patient or clinician measurement based care dashboards. There is much also to be gained in the use of the data generated from a number of digital tools in themselves, with more sophisticated analytical methods.

> **"We are nowhere close to other areas of medicine when it comes to the use of digital tools. We can use them for prevention, diagnosis and treatment, and yet we haven't even scratched the surface regarding the possibilities to support mental health through digital tools. These include using wearables, mining data from the electronic health record and beyond, apps, virtual reality, and beyond.**
>
> - Dr. Gillian Strudwick, *Lead, Digital Mental Health Lab*

Groundbreaking Research Underway in the Digital Mental Health Lab:

Hope By CAMH CAMH and University of Oxford (UOxford) are partnering to work on the suicide-related health tool known as the Hope App to support effective and equitable suicide care planning and prevention. The partnership, including CAMH, UofT, Oxford Health Foundation Trust (OHFT), and UOxford, will leverage the Hope App and existing projects to engage clinicians and better utilize technology to support patients and families. This work will be guided by the following aims: 1) identify the help-seeking needs of diverse populations in relation to suicide care; 2) develop a shared suicide care planning tool (Hope App) that is grounded in health equity and data collection capabilities; 3) improve understanding of the processes, workflows and needs to integrate the use of digital suicide care planning tools into clinical care workflows; and 4) examine the feasibility and impact of deploying digital suicide care planning tool (Hope App) into Canadian and UK care and community settings.

BeWell at CAMH BeWell is a two-way text-based population mental health intervention, which has been implemented and evaluated as a mental health support for Saskatchewan residents during the pandemic and a mental health support for post-secondary students at Georgian college. As part of an organizational strategic initiative to support clinician well-being, the BeWell intervention has been adapted to support clinicians at CAMH. Through a participatory research design, the BeWell program was designed, developed and implemented in partnership with a group of clinicians (social workers and occupational therapists) at CAMH. In this context, BeWell aims to support social workers and occupational therapists' well-being by connecting them to curated mental health resources, psycho-educational tools, supportive motivational messaging and professional development opportunities and events through a 12-week two-way text messaging program.

IDEA Study This project engages nurses in generating ideas on how to support and optimize nurses' experiences with CAMH's Electronic Health Records (EHR) system, thereby improving efficiency and reducing EHR-related burden. The specific aims of this research are to 1) evaluate the utility of the analytics platform to accurately capture the EHR utilization pattern of nurses; 2) understand the utilization patterns and user experience of nurses in the EHR; 3) identify areas for improvement in the utilization of the EHR for documentation; 4) generate potential interventions to improve efficiency of nurses' EHR use; and 5) rank and reduce intervention options through nurses' assessment of relevance, feasibility, and perceived impact. This work creates a direction forward on how we can address nurses' EHR-related burden and burnout and gain greater utility of EHR systems for nursing professional practice. The project findings will inform the co-design and implementation of interventions to improve the EHR. This study aims to address causes of burnout and time inefficiencies amongst nursing professionals. If effectively addressed, this could lead to the delivery of safer, efficient, and improved mental health care.

KCNI-Developed Data Platform Will Help Identify the Links Between Brain and Heart Disease

Heart disease is the number one killer worldwide, and brain/mind disorders, such as depression, are the third leading cause of mortality in Canada. Together, brain-heart diseases affect over six million Canadians. Research and clinical observations are uncovering that there are major linkages between these diseases, including how they develop and progress. For example, patients with heart failure are at increased risk for depression, cognitive impairment and sleep disorders, which increases poor patient outcomes such as death. Yet despite this, brain and heart conditions are treated clinically today as separate entities, even when co-occurring in the same patient.

Established in 2021, the Hub in Cardio-Neuro-Mind Research (HCNMR), led from the University of Ottawa, aims to undertake research to ultimately transform the care of patients with heart and mind conditions. Outcomes of their research include understanding how brain and heart diseases co-occur and affect progression of disease. This will lead to new screening tools for early detection, and new drugs and psychological therapies to treat brain-heart diseases. The HCNMR team's research will pioneer a patient-centred NeuroCardiac Care Model, where all heart patients are screened for brain diseases and treated with consideration to both conditions (and vice versa for brain disease patients).

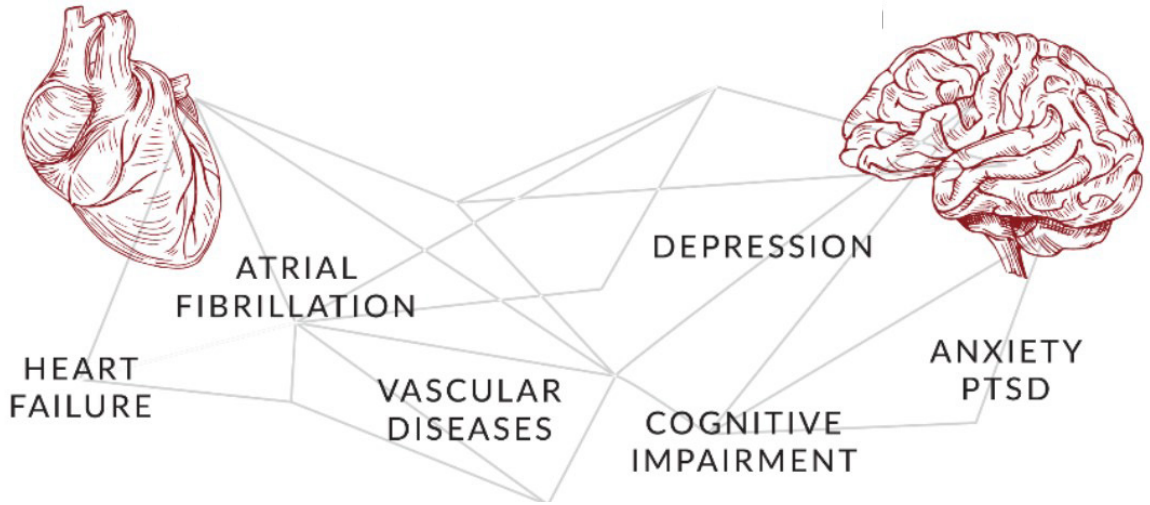
In the spring 2023, the Krembil Centre signed an agreement with the HCNMR to lead the technological development of a customized data platform to support multi-modal research for the Heart and Brain. Called the Cardio-Neuro-Mind Data Platform, this will serve as a repository for HCNMR generated data supporting the identification and validation of biomarkers (imaging, blood, etc.) to characterize the co-occurrence of

psychiatric, cognitive and cardiac symptoms, identify common underlying disease mechanisms and at-risk phenotypes, and inform the development of novel therapeutic targets and interventions.

Based on the novel Neuroinformatics Platform and BrainHealth Databank governance developed at KCNI, the system will serve researchers at the University of Ottawa, Heart Institute, Royal Hospital and Élisabeth Bruyère Hospital. Led by David Rotenberg, this cutting-edge platform expands key data capabilities and offers an opportunity for collaboration across disciplines and hospitals towards brain-health and brain-heart nexus discovery.

"Current medical practice treats brain-heart conditions as siloed entities, with limited awareness of their tight interactions in pathogenesis, shared risk factors, mutual regulation, and potential shared solutions. Together we are now poised to address this knowledge gap and seek innovative solutions to improve patient care."

- Dr. Ruth Slack, *PhD, co-lead of HCNMR*



The Impact of Cultural Models Of Addiction and Motherhood: A Cross-Cultural Study

This fall, Drs. Laura Sikstrom and Sara Ling, scientists at the Krembil Centre, will kick off an international, multi-site study that focuses on how cultural models of addiction and motherhood impact psychological well-being and other recovery indicators in mothers. The project will take place at treatment centres in Canada, the Netherlands and England.

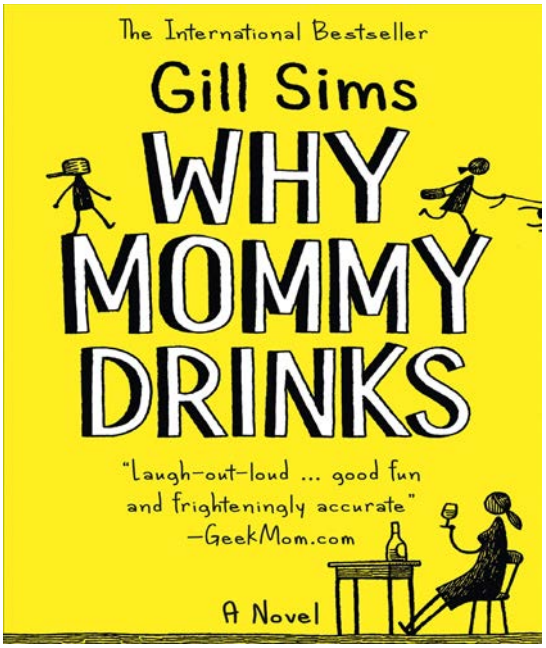
Ultimately, Drs. Sikstrom and Ling's aim is to reduce the stigma and increase knowledge about drug use in motherhood across the study populations by generating information about the role cultural models of addiction and motherhood have on harm reduction and recovery outcomes. The research will inform cross-national discussions with legislators and other experts that aim to reduce barriers to care for women.

"Sara and I first started talking about motherhood and addiction when Sara noted barriers to care for mothers," says Dr. Sikstrom. "I mentioned a service in Alberta—where I am from—that houses mothers and their young children during medical withdrawal, since they found that women didn't access care unless they took a family-centred approach. We thought this was an important area to examine, especially with a prevalent 'mommy drinks because…' culture in both North America and Europe."

Together with scholars from Brunel University in England and The University of Amsterdam in the Netherlands, Drs. Sikstrom and Ling will collaborate with Dr. Caitlyn Placek, an associate professor in the Department of Anthropology at Ball State University in Muncie, Indiana. Dr. Placek was recently awarded a Fulbright Global Scholar Award to spend time in each host country over a six-month period in the coming year, starting at the Krembil Centre in October. At each site, Dr. Placek will share data from recent efforts in the United States that have successfully improved harm reduction and recovery indicators in women of childbearing age seeking treatment for opioid and substance use disorders.

This project focuses on these high-income countries because they are similar in terms of gender parity, and opioid and substance use have reached epidemic proportions in each, including deaths due to drug overdoses and drug-related hospitalizations. All three countries have a mission to reduce illicit drug use and have increased governmental funding to tackle drug-related issues; however, each is taking a slightly different approach (e.g., drug legalization, supervised consumption sites, etc.) It is expected that this study will facilitate cross-national insight into which treatment approaches are working, and how cultural models influence psychological well-being, harm reduction and other indicators among mothers and women of childbearing age.

The information gained from this study will be collated and disseminated through a series of virtual panels and public talks with legislators and other interested parties. In addition, the findings from this study will inform other research initiatives led by Drs. Ling and Sikstrom that are under review from funding agencies, e.g. CIHR, that will explore using digital tools (like mobile apps) to provide more gender responsive substance use services.



An example of a typical humourous gift given at a baby shower for expectant moms.

Hypotheses to be tested in this study:

1. Women who view addiction as a moral failing will be more likely to hold negative views about their recovery, will have lower scores on mental health scales, and will be less likely to engage in harm reduction behaviours.
2. Women who hold traditional views of motherhood will have worse recovery outcomes, lower scores on mental health scales, and will be less likely to engage in harm reduction behaviours.
3. Women who view addiction as a brain disease will be more likely to hold positive views about their recovery, will have higher scores on mental health scales and will be more likely to engage in harm-reduction behaviours.
4. Women who view addiction as caused by biopsychosocial factors will be more likely to hold positive views about their recovery, will have higher scores on mental health scales, and will be more likely to engage in harm reduction behaviours.

Leveraging Donor Funding to Advance Research

Dr. Etay Hay's research team is among the foremost in the country using computational models of cortical circuits to study the cellular and circuit mechanisms of cortical processing in health and disease. His team's work is recognized nationally and internationally, particularly through his success in obtaining competitive peer-reviewed grants. This past year, Dr. Hay applied for three grants focused on research of the neurobiology of depression to improve diagnosis and improving early detection of schizophrenia in youth. His successful applications were ranked at the top of those submitted and this funding will help the team obtain new results and papers that will form the basis of larger applications to agencies like the Canadian Institutes of Health Research and the National Institutes of Health in the US.

Krembil Foundation funding was vital to his success, since it was the primary mode of supporting his trainees (one postdoc, two graduate students) for three to four years to obtain the results and publish the papers on which the grant applications were based. The grants are outlined below:

Labatt Catalyst Fund

In collaboration with Drs. Tarek Rajji and Heather Brookes, Dr. Hay and his team will apply computationally-derived biomarkers to estimate the level of cell-specific inhibition from patient electroencephalograms (EEG) and test if it's linked with cognitive impairment in aging.

Labatt Postdoctoral Fellowship

In collaboration with Drs. Etienne Sibille and Thomas Prevot, Dr. Alexandre Guet-McCreight (a postdoctoral fellow in Dr. Hay's lab) will use detailed brain network models to predict the dose of new drugs for depression (developed at CAMH) given EEG biomarkers of depression severity. The project will pioneer in-silico drug testing and supports a recent patent that aims to facilitate translation of the new compound to clinical use.

For the above two studies, the team found on a separate dataset that a significant proportion of depression patients show the EEG biomarkers of reduced SST interneuron inhibition, and the estimated level of inhibition is correlated with their depression score. This is in line with the hypothesis of the studies.

Miner's Lamp Fund

In collaboration with Drs. Andreea Diaconescu and Michael Kiang, Dr. Hay and his team will apply computationally-derived biomarkers to estimate the level of cell-specific inhibition from EEG of young patients at-risk of psychosis and use it to improve early detection of psychosis/schizophrenia. The team is at advanced stages of achieving the main aim of predicting the dose response of the new drug based on the EEG biomarkers of SST inhibition loss (depression severity).

The BrainHealth Databank: Creating A Learning Health System

Now in its fifth year, the BrainHealth Databank is on its way to becoming the single largest digital repository of mental health data in Canada. Over the past year, the BrainHealth Databank team, led by David Rotenberg, has been striving to create a Learning Health System that will improve patient care and enable discovery and innovation. A Learning Health System integrates research and clinical care to create a cycle of continuous improvement and discovery, and innovation.

The BrainHealth Databank continues to collect data and biological samples (through the Biobank) that is made available to researchers at CAMH and around the world for re-use in research. The BrainHealth Databank is on its way to becoming the single largest digital repository of mental health data through support of projects like the Major Depressive Disorder Integrated Care Pathway studies and the Toronto Adolescent and Youth (TAY) Cohort study.

The BrainHealth Databank has worked closely with stakeholders to develop a standardized consent for prospective data re-use for secondary research, currently being finalized by the Research Ethics Board (REB).

The BrainHealth Databank team has drafted procedures and supporting documentation that is currently under review by the REB. These documents were produced with extensive input from stakeholders across the CAMH, including the Research Office, CAMH Researchers, Patient and Family Advisors and the Research Executive Committee. This ensures these procedures reflect the needs of the CAMH. The governance policy for the BrainHealth Databank will be approved by the end of 2023.

The BrainHealth Databank is supporting data and biological sample management of 3,000 youth seeking mental health services for the TAY Cohort Study. To date, it has:

391 biosamples including **64** microarrays, managed through the Biobank and LabKey

500 participants assessed clinically through REDCap

510 MRI sessions managed through XNAT

384 respiratory sinus arrythmias stored as time series data

Digital Front Door: Improving Pathways to Care

The BrainHealth Databank team—in collaboration with patients and families, clinicians, administrators, technology experts, researchers and vendors—is advancing the development and implementation of a Digital Front Door platform to digitize the patient journey and to support integrated measurement-based care (MBC). The purpose of the platform will be to enable a single-point of entry for CAMH patients and families to receive information and services, relating both to their clinical care and participation in research. Launching later in the fall, the platform will align with measurement-based care as well as virtual care, and include features seen in traditional patient portals.

Looking Forward

The BrainHealth Databank is driving discovery and innovation by accumulating data from care and research while laying the foundation to integrate artificial intelligence into the clinic to advance personalized treatment. Over the coming year, the team will be advancing the following initiatives:

- extend the BrainHealth Databank beyond the walls of the CAMH;
- continue deployment of digital MBC and actigraphy for sleep measures across the hospital;
- expand wearable services and integrated wearable and biomarker collection;
- enhance AI pipelines for personalized care and pilot implementation in clinics;
- become world leaders in Open Science in mental health; and
- expand international collaborations.

KCNI scientists Drs. Michael Wainberg and Shreejoy Tripathy.

CAMH BrainHealth Databank, By the Numbers:

85+

CAMH Stakeholders

CAMH-Wide BrainHealth Databank Team
Steering Committee, Working Groups and Operational Teams

11

External Scientific Advisors
Local, national and international experts in digital health technologies, Learning Health Systems and large-scale data initiatives

14

Patients, Families, & Lived Experience Advisors Engaged
Co-design and participation in aspects impacting patient care and experience

11 **Collaborative Awards**
Including grants and fellowships

12 **Trainee Projects**
Led by residents, postdoctoral fellows, PhD, Masters and undergraduate students

Visit the BrainHealth Databank website

CREATING IMPACT BEYOND CAMH

KCNI Data Analytics Will Be Used to Save Lives

Beginning on November 30, 2023, people across Canada will be able to call and text 9-8-8, a new three-digit service, for help when they are facing their most challenging moments. CAMH is leading and coordinating the national rollout of 9-8-8, which will be available in French or English, 24/7, 365 days a year to any person living in Canada who is thinking about suicide, in emotional distress, or who is worried about someone they know.

The CAMH data team is leading the data and analytics implementation of 988. Integrating new pan-Canadian technologies, the team is creating a centralized database to support analytics and reporting across the Canadian network. The team has developed capacity predictions and operational analytics for the roll-out this November.

A New Start-Up Focused on Improving the Patient Experience

Kelello Health is an early-stage start-up, created through KCNI, that uses an AI-powered approach to help individuals and clinicians monitor mental health trends and provide state-of-the-art support when care is needed. The goal is to improve the patient experience and create seamless processes to deliver high quality mental health care.

Co-designed with patients, the scalable Kelello Health platform provides a user-friendly interface to track and visualize trends in mood, medication, health data, activity, and sleep, giving individuals personalized feedback and directing them to local clinical support as needed. With a single click, the platform provides qualified health professionals with a visual patient summary and clinically-validated personal treatment recommendation and risk factors, leveraging extensive mental health data.

Kelello Health aims to empower the individual in managing their own health care journey, while providing clinicians with detailed patient profile and advanced AI-driven guidance to provide best-in-class mental health care. Currently serving 16,000 patients, the platform is being scaled for deployment at other hospitals, clinics and practices.

Creating a Groundbreaking, Pan-Canadian Youth Mental Health Data Platform

Launched in October 2022, the Canadian Youth Mental Health Insight Platform (CYMHI) is a first-of-its-kind Canada-wide cooperative effort between youth mental health stakeholders across the spectrum, especially youth and their families. The result will empower the sharing of and learning from mental health data to better prevent, diagnose and treat youth mental illness in Canada.

CAMH leads the pan-Canadian team that was awarded a $5.13-million grant for this project over three years via a 2021 open call for applications to the Brain Canada Youth Mental Health Platform, powered by RBC Future Launch, with support from Power Corporation. When launched, the interactive web portal will enable knowledge sharing in creative new ways, enabling precision modelling to predict the future needs of individual youth and help them and their families make decisions about their care.

Over the past year, several key positions have been recruited, including a data engineer, development operations engineer, project manager and senior project manager to support the work. The team is also nearing finalization of an extensive procurement process for the underlying data fabric that will enable the CYMHI platform.

Using KCNI Computer Models to Understand the Potential of and Biomarkers for New Treatments

Damona Pharmaceuticals is a preclinical pharmaceutical company founded by Dr. Etienne Sibille, Deputy Director of the Campbell Family Mental Health Research Institute at CAMH. Damona's mission is to discover and develop small molecules for the treatment and prevention of cognitive symptoms in depression and other brain disorders. The KCNI laboratories of Drs. Etay Hay and Shreejoy Tripathy are collaborating with Damona to develop electroencephalogram (EEG) (Hay Lab) and genetic (Tripathy Lab) biomarkers for the drugs developed at Damona, using computational models.

In Dr. Hay's project, he is testing the ability of a new drug called α5-PAM, which boosts the connections of certain brain cells that are linked to depression. α5-PAM was previously shown to exhibit antidepressant and pro-cognitive effects in rodent models of chronic stress, but it is not known how α5-PAM affects the human brain because it currently cannot be tested in the living human brain.

Working in collaboration with Damona scientists, Dr. Hay used detailed computer models to simulate α5-PAM's effects on human brain cells and networks. The simulations showed that α5-PAM can recover function in depression brain networks. The project also identified biomarkers in EEG brain signals that can predict dose response and help measure the drug's efficacy. This information will facilitate the development and testing of α5-PAM for clinical translation and depression treatment.

Dr. Tripathy is collaborating with Damona to better understand changes in brain cells as people age into late life. Currently, a major challenge limiting the development and application of therapies for brain disorders is the inaccessibility of the human brain for diagnostic biopsies. Unlike in conditions such as cancer where biopsies often guide life-changing treatments, it is challenging to link an individual patient's brain disorder to its underlying cellular cause. As a result, disorders like major depression with effective treatments can require multiple rounds of trial and error to find fruitful drugs and dosing strategies for each patient.

This project aims to discover biological factors that govern why some individuals are more likely to have dysfunction of certain types of neurons as they age. By using brain tissue collected from donors after their death, they will begin to unravel the causes of such cellular changes by comparing different groups of people, like those who have specific genetic variants or those who had a brain disorder during their lives.

Dr. Tripathy and his collaborators will apply this knowledge to develop biomarkers that can predict a patient's degree of neuron-specific vulnerability using simple, routinely-accessible assays, like genetics and brain imaging. Dr. Tripathy will ask how increased risk for dysfunction of specific neuron types may underlie cognitive decline and other behavioral changes in late life. They ultimately aim for these approaches to deliver on the promise of personalized medicine for brain disorders by helping guide treatment decisions in the clinic.

KREMBIL CENTRE TEAM UPDATES

COMPUTATIONAL GENOMICS TEAM

TEAM LEAD: DR. SHREEJOY TRIPATHY

The Computational Genomics team comprises a diverse group of 11 research staff, graduate students, and undergraduates. The team pursues a range of questions at the heart of fundamental neuroscience and mental illness, such as: how has neuron diversity expanded over primate brain evolution? What genetic and environmental factors make some types of neurons especially vulnerable in late life? And developing new personalized medicine approaches for better guiding new neuropsychiatric therapies to the right patients.

Since our previous reporting, the team has published 12 papers and presented at multiple local and international conferences, spanning Toronto and Montreal, to San Diego and Barbados. The team continues to cultivate a wide network of world-leading collaborations with colleagues in Germany, the UK and the US, and includes research in cutting-edge experimental and methodological techniques and innovations in clinical practice.

One recent project that we are especially proud of is work led by Shu'ayb Simmons, who recently defended their Masters of Science in August 2023. The goal of Shu'ayb's project was to better understand the molecular mechanisms in the brain that contribute to racial disparities in schizophrenia illness courses, for example, why Black individuals with schizophrenia typically experience earlier onset and more debilitating symptoms relative to white individuals. Our hypothesis was that these differences might in part be related to race-associated social stressors, such as anti-Black racism, systemic poverty, and societal, neighborhood and institutional adversities.

Using genome-wide gene expression data collected from the brains of almost 800 Black and white individuals comprising those with schizophrenia and healthy controls, Shu'ayb conducted a series of comprehensive analyses to assess biological differences associated with race and with schizophrenia. Our analyses revealed that the brains of Black individuals are markedly different from those of white individuals, with differences related to cellular stress and immune-related functions. Moreover, the biological signature of schizophrenia differed between races, which suggests there are differences in metabolism and neuroimmune function. In total, this study contributes to the growing body of literature addressing health disparities and underscores the necessity of considering race-specific factors in neuropsychiatric research.

> **"Psychiatry and neuroscience have always impassioned me. As I have engaged more with psychiatric research, the prominent racial disparity within the field has stood out to me. This disparity is inequitable for Black health and largely caused by poor consideration of race and neglect to include racially diverse data. With my current research, I am able to merge my passions – neuroscience, genetics, and equitable health outcomes – with a lot of bioinformatics as the cherry on top.**
>
> - Shu'ayb Simmons, *Master's Student, Computational Genomics Team*

BRAIN CIRCUIT MODELLING

TEAM LEAD: DR. ETAY HAY

The Brain Circuit Modelling team has received a postdoctoral fellowship and two federal graduate awards. One master's student will defend her thesis in the fall, and another will transfer to PhD. An undergraduate member received another competitive summer award to finish his research in the lab, and got accepted to a prestigious medical school. This has enabled the team to continue driving forward existing projects, while also embarking on new ones.

In the past year, Dr. Hay and his team published a paper in *PLoS Computational Biology*, using detailed in-silico simulations of the lab's human cortical microcircuit models to characterize the first cell-specific EEG biomarkers of altered Somatostatin (SST), a hormone that regulates a variety of bodily functions interneuron inhibition in depression. The paper was published open-access, and the team has shared the models and code openly with the scientific and general community. Dr. Hay received a grant (in collaboration with Dr. Tarek Rajji from CAMH and the PACt-MD group) that aims to apply the in-silico biomarkers on patient EEG data to test the role of SST interneuron inhibition in linking a history of depression with cognitive impairment in aging.

The team finished another project that characterized the EEG biomarkers of altered inhibition from a different cell-type (PV interneurons) in schizophrenia. The work links different levels of inhibition and EEG biomarkers of schizophrenia severity. The lab published a preprint describing the results, which will be submitted to peer review. Dr. Hay received a grant (in collaboration with Drs. Andreea Diaconescu and Michael Kiang from CAMH) that aims to apply the in-silico biomarkers on youth patient EEG data at-high-risk of psychosis and schizophrenia, to improve patient stratification and early detection.

The team also filed a new patent based on a collaborative project with Drs. Etienne Sibille and Thomas Prevot from CAMH (highlighted earlier in this report). They developed and applied a computational platform to test new pharmacology (developed at CAMH) on human microcircuits and cortical processing in-silico, to identify EEG biomarkers for drug monitoring and thus support translation of the drug to clinical use. The team submitted a paper of the results to peer-review and is working on a follow-up project to predict drug dose based on in-silico EEG biomarkers of depression severity.

WHOLE BRAIN MODELLING

TEAM LEAD: DR. JOHN GRIFFITHS

Whole-brain modelling at KCNI has moved forward on its research program agenda in several important ways during the 2022-2023 academic year. The primary focus of the research group at CAMH and the University of Toronto is to advance our understanding of the neurophysiology of noninvasive brain stimulation, from the perspectives of both basic science and of applied clinical therapeutics. We pursue this goal using mainly computational and mathematical modelling techniques, closely integrated with novel experimental neuroimaging and brain stimulation experiments in patient and non-patient populations.

Last year, the team introduced a new technical innovation to this field by implementing our neurophysiological models in new industry-standard programming environments developed for deep learning. This advancement has significant advantages by allowing automatic differentiation-based parameter estimation algorithms. The team has extended this model-fitting approach beyond its initial application for fMRI data to the domain of evoked responses in EEG, including those elicited from single-pulse transcranial magnetic stimulation (TMS). This latter work constitutes the best-in-class demonstration of personalized whole-brain network modelling for task-based neurophysiological brain activity measurements within the field to date. More recently, the team has made progress in incorporating stronger biophysical and anatomical constraints on our whole-brain models, focusing on the important question of individual variability in TMS target connectivity using a combination of electromagnetic field modelling and whole-brain high-density anatomical and functional connectivity analyses.

Other key articles from the past year include an investigation into negative correlations in resting-state fMRI that are driven by both local and global brain dynamics, led by PhD student Shreyas Harita, and a paper on modelling rTMS-induced metaplasticity dynamics within oscillatory corticothalamic circuits with PhD student Kevin Kadak and Dr. Griffiths. This and other work has been presented by lab members at major national and international conferences, including the Society for Neuroscience (SFN 2022), Organization for Human Brain Mapping (OHBM 2023), Society for Functional Near Infrared Spectroscopy (SFNIRS 2022), and Canadian Neuroscience Association (CAN-ACN 2022).

As well as presenting their work, several members of the group have taken leadership roles in organizing local, national, and international scientific meetings. In June, the team took part in

the annual KCNI Summer Academy, where members of the lab supervised young trainees on a week-long neuroimaging and computational modelling research project, and Dr. John Griffiths gave a talk on computational modelling of noninvasive brain stimulation connectivity, plasticity, and in-silico testing of personalized therapeutic interventions. In July, post-doc Dr. Davide Momi ran a full-day educational course at OHBM 2023 about principles and applications in whole-brain, connectome-based models of brain dynamics. This event also featured doctoral student Sorenza Bastaens giving her first major conference presentation, alongside a list of world leaders in the field. Drs. Griffiths and Momi also held a well-received symposium at OHBM on recent advances in whole-brain, connectome-based neurophysiological modelling of brain stimulation.

Finally, the group has continued its success in securing grant funding from competitive national competitions. This includes a CAMH Discovery grant for computational modelling of TMS-EEG brain network dynamics in depression, as well as a Canada Foundation for Innovation (CFI) grant providing centre-wide funds for new computer hardware and also new mobile neuroimaging (fNIRS) hardware, to be used in the EEG lab at CAMH's College Street site. Several lab members have also been successful in obtaining funding for PhD scholarships, summer internships, and travel grants.

COGNITIVE NETWORK MODELLING

TEAM LEAD: DR. ANDREEA DIACONESCU

The academic year 2022–2023 represented a period of exponential growth and consolidation for Dr. Andreea Diaconescu's research program, the Cognitive Network Modelling Group. The group has cemented its position as a leader in the burgeoning field of computational psychiatry with a particular focus on early detection and prevention of severe mental illnesses, such as schizophrenia and major depression.

During this period, the team was prolific in producing high-impact publications. Three landmark papers focused on applying mathematical models for better understanding the neurobiological basis of schizophrenia, the computational underpinnings of major depression, and the use of machine learning algorithms for early detection of mood disorders. These publications were featured in esteemed journals such as *Nature Neuroscience*, *JAMA Psychiatry*, and *Biological Psychiatry*, thereby ensuring a wide readership and substantial scientific impact.

As a respected thought leader in the field, Dr. Diaconescu presented at several high-profile conferences. Noteworthy presentations included invited talks on Cognitive Network Modelling at both the Computational Psychiatry Symposium in Iowa and the Krembil Centre for Neuroinformatics Open House in Toronto. Other presentations covered cutting-edge topics like the clinical potential of cognitive network modelling, advanced fMRI techniques and the effects of psychedelics on brain connectivity. These talks were delivered at international conferences, including the Society for Schizophrenia Research, thereby facilitating collaboration.

Under Dr. Diaconescu's mentorship, trainees (postdoctoral fellows, PhD and Master students) have showcased their work at various international conferences. These presentations cover an array of topics, from the challenges of measuring individual differences in computational psychiatry to the use of computational models in understanding symptoms and behaviors in clinical populations. Specifically, studies were presented at the Organization for Human Brain Mapping, Society of Biological Psychiatry, and the Society for Schizophrenia Research, among others.

The team also successfully acquired multiple grants, bringing in a total of $1,214,000 for the period of 2022–2025. Notably, these grants focus on diverse, yet interconnected areas:

- stratification of risk for schizophrenia using cell-specific EEG biomarkers;
- exploring the potential of psilocybin for treatment-resistant depression in autism; and
- infrastructure support for advancing personalized computational modelling in youth mental health.

Each of these grants represents a strategic alignment with the team's overarching objective: to utilize computational models for improving mental health diagnostics and treatment. Taken together, these achievements not only underscore the team's commitment to advancing the field of computational psychiatry but also promise to catalyze future research endeavors aimed at mitigating the societal burden of severe mental illnesses.

WHOLE PERSON AND POPULATION MODELLING

TEAM LEAD: DR. DANIEL FELSKY

In 2022-2023, the Whole Person and Population Modelling team celebrated multiple landmark achievements, including reaching a total of over $25 million in external funding (including PI roles on a Canadian Foundation for Innovation Grant to improve the KCNI computational infrastructure) as well as a record 10-abstract showing, including an oral presentation, at the Society of Biological Psychiatry's Annual Meeting, where eight trainees joined Dr. Felsky in San Diego to present their original Whole Person Modelling research on the international stage.

In total, the team had more than 45 peer-reviewed local, provincial, and international abstracts and talks accepted. The team published 13 papers (11 peer-reviewed), including an invited review at Discover Mental Health titled "Whole Person Modeling: A Transdisciplinary Approach to Mental Health Research," which puts our ethos, methodologies and ideas for the field on the map.

Dr. Felsky was awarded the Researcher Prize at the University of Toronto's Department of Psychiatry Research Day. He was also invited to join the Rotman Research Institute, Baycrest Hospital, as an Adjunct Scientist, as well as the University of Waterloo, also in an adjunct role, as Assistant Professor. These positions have increased the influence and visibility of KCNI at other institutions, and has resulted in new mentorship and research opportunities. Progress continues unabated, with 25 papers currently in review and revision, and an additional 13 papers nearing submission.

In total, the Whole Person Modelling group had 21 new and returning trainees pass through its doors in 2022-2023. Trainee accomplishments continue to exceed expectations:

Dr. Mohamed Abdelhack was awarded a Simons Collaboration on the Global Brain (SCGB) Conference Award for his Arabs in Neuroscience Summer Program; Mai Gamal is currently enjoying her four-month L'Oréal-UNESCO for Women in Science Egypt Young Talents Program Travel Scholarship in the lab; Denise Sabac won the prestigious Canada Graduate Scholarship – Master's for her work in subtyping mental illness in youth; Earvin Tio secured his second Ontario Graduate Scholarship; and Tara Henechowicz won the Data Science Institute Doctoral Student Fellowship.

In addition, Dr. Felsky was invited to serve as mentor for three new Strategic Training for Advanced Genetic Epidemiology (STAGE) Program trainees, all of whom were successful in their fellowship applications. The STAGE program offers training and career development opportunities designed to cross-train individuals at the interface of genetics and population health sciences in genetic epidemiology and statistical genetics.

At the end of the summer in 2023, two MSc students will be graduating with Dr. Felsky as sole supervisor: Rachel Bercovitch (who successfully defended her thesis on August 15 and was nominated for a dissertation award for outstanding scholarly contributions) and Mu Yang. Rachel has accepted a position working as a Bioinformatician at Mt. Sinai Hospital in New York and Mu Yang will be training in clinical trials research for the next year as the recipient of a prestigious Canadian Network for Statistical Training in Trials Fellowship (valued at $70,000 for a master's level graduate).

DIGITAL HEALTH & ARTIFICIAL INTELLIGENCE TEAM

TEAM LEAD: RECRUITMENT ONGOING

In pursuit of CAMH's commitment to improving care experiences using data-driven support, KCNI is operationalizing machine learning (ML) and artificial intelligence (AI) to further assist our physicians, nurses, operational staff and researchers in various use cases across the hospital. As the central data hub for CAMH and with our expertise in big data and analytics, this makes us exceptionally positioned to be the hub for ML and AI development.

To do so, the Health Intelligence team was established earlier this year. This cross-disciplinary group will intake all potential ML and AI use cases at the hospital and work closely with all groups that may be impacted by said use cases, including physicians, patients and more. The team has been working with subject matter experts in various fields, such as health equity, to develop protocols to minimize potential bias in the developed algorithm at all stages. Furthermore, our gated governance procedures will ensure that, throughout the development of our algorithms, there are regular checkpoints to assess their fairness and equity.

Within Health Intelligence, the Machine Learning Operations team, or MLOps for short, has developed the operational infrastructure that the ML and AI algorithms will use, with core tenets modelled directly after the FAIR guiding principles for scientific data: findable, accessible, interoperable and reusable. Any prediction produced by our algorithms must be logged and able to be audited to improve their accuracy and performance that meet our standards–our systems will fully enable that, with full transparency through most, if not all protocols on how we developed these algorithms and what affects their predictive abilities. With these guiding principles in place and flexible yet robust infrastructure, our MLOps team can facilitate real-time predictions using various kinds of data and further enabling a data-driven approach to mental health care.

A rendering of the planned Research & Discovery Centre, future home of the Krembil Centre for Neuroinformatics.

Since the inception of Health Intelligence, we have taken on three projects, each serving various aspects of CAMH, encompassing research, operations and quality improvement. Their brief descriptions are as follows.

Research: Major Depressive Disorder and Alcohol Dependence-Integrated Care Pathway (MDDAD-ICP) – Patient Dropout Prediction Algorithm

The MDDAD-ICP, one of CAMH's first integrated care pathways, helps map out a treatment process for patients diagnosed with major depression and alcohol dependence. Some patients drop out midway through their treatment plan, which can affect their pathway to recovery. The team is developing an algorithm with the MDDAD-ICP that predicts if a patient within the ICP may drop out through the program. This algorithm will assist the study team in identifying the patients likely to drop out of the care pathway and plan better for their treatment to retain them to further assist in their care.

Operations: Emergency Department Volume Prediction

The emergency department (ED) is often the first place for patients who are experiencing distress. However, they may not be treated promptly upon arrival due to how busy the ED is. To improve their wait times at the ED and subsequently the quality of care offered, the team is currently working with the ED team to predict, on a given day, how many patients may visit the ED. The developed algorithm would help the ED staff schedule the appropriate number of nurses and physicians, which would help account for surges in patient visits that can overwhelm the ED.

Quality Improvement: Clinical Note Extraction Using Natural Language Protocol

Clinical notes are critical in capturing key information from patients during their visits to CAMH. Currently, these notes are stored in an "unstructured" format, meaning that the raw-text data are often stored as. This makes the text difficult to analyze compared to more traditional, structured data. To transform raw-text data into a more structured format, the team will use natural language processing algorithms that extract key text, such as patient sentiments and medical terms. This data will then become accessible as another key resource to improve the quality of care and research at CAMH.

EVENTS AND KNOWLEDGE SHARING

This year saw the Krembil Centre for Neuroinformatics continue to advance its position as a leader in supporting global knowledge sharing through Krembil Centre-led initiatives and bridging existing knowledge gaps in neuroinformatics through participation in collaborative learning events.

KCNI Summer Academy

Building on the success of previous years, from July 10-14, members of the KCNI team hosted up-and-coming scientists for Krembil Centre for KCNI Summer Academy. The Summer Academy is open to Graduate Students, Post-Graduate Research and Clinical Fellows, as well as Early-Career Scientists from across Ontario with interest in learning more about Neuroinformatics, encompassing genetics, cognition and brain structure and function.

A total of 21 people participated this year. This unique opportunity aims to prepare participants to handle and analyze multiple data types in hopes that their own research may benefit from collaborative and multi-modal approaches. Critically, participants also learned about best practices for data management and quality control in the context of integrative analysis. Based on positive feedback from last year's participants, organizers once again offered a hands on "learning by doing" approach to the week.

Participants were split into three groups where they were mentored by KCNI scientists as they completed intensive group projects matched to their interests over the course of the week. Students presented their group project to the group at the conclusion of Project Week. Participants heard from thought leaders in the field, including attending a talk at SickKids Hospital.

Project 1: Single Cell Transcriptomics

Integrative analysis of human single-nucleus gene expression datasets: How are neocortical cell types defined by gene expression and how do cells' gene expression patterns change in Alzheimer's disease?

Lead scientist: Dr. Shreejoy Tripathy

What's this project about?

Perform integrative analysis of human neocortical cell types according to transcriptomics, which is the study of the "transcriptome," the complete set of all RNA molecules expressed in a given entity, such as a cell, tissue, or organism.

Positive feedback from Summer Academy participants:

> I found using different software to process data was very helpful. I learned lots of new coding techniques and actually understood what each command contributed to when processing MRI images and combining different predictors of MDD to assess which ones are higher contributors.

> The ratio of TAs to students was very useful and allowed for both group and personalized learning.

> I got to meet many people and explore career opportunities in the field of neuroinformatics.

> It was really useful that we not only worked on RNA-sequencing and coding and but also integrated real life data. This enabled me to better understand the concept and ask many more questions which I believe helped me greatly in getting better at analyzing the data.

Project 2: Transdisciplinary Mental Health Modeling with Machine Learning

From domain-specific data to transdisciplinary models: an exercise in whole-person modeling from feature engineering to model explanations.

Lead scientist: Dr. Daniel Felsky

What's this project about?

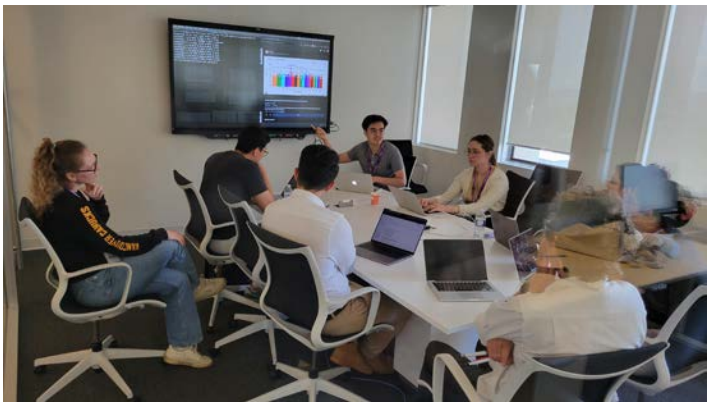
Building a transdisciplinary machine learning model to predict risk for mental illness in a large simulated human population dataset. This will involve exposure to genetic, neuroimaging, and sociodemographic data types and their integration.

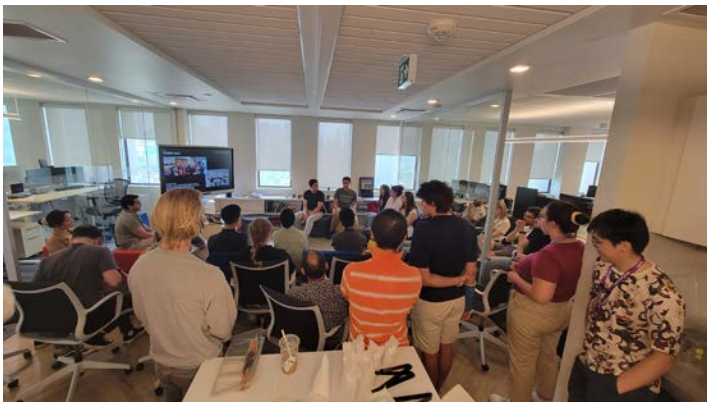
Project 3: Whole-Brain Modelling of Non-Invasive Neurostimulation Therapeutics and Neuroimaging Connectomics

Lead scientist: Dr. John Griffiths

What's this project about?

Use neuroimaging-based computational models of transcranial magnetic stimulation (TMS) brain stimulation to investigate the micro-physiological and macro-network effects of TMS therapies used in psychiatry and neurology.





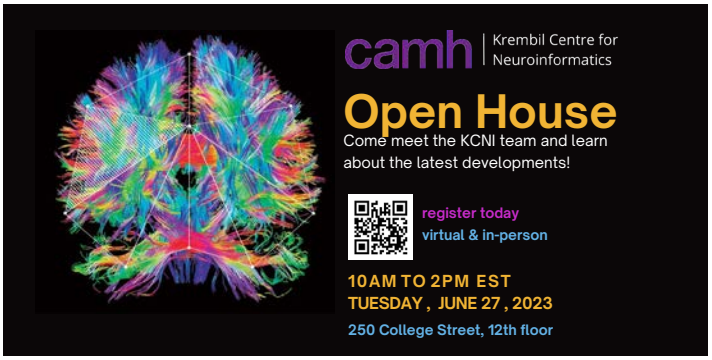
KCNI VIRTUAL SUMMER ACADEMY

Complementing the in-person Summer Academy, from June 19 to 23, KCNI published a free, globally accessible webinar series focused on working with the clinic to perform integrative multi-scale neuroscience data analysis. The series was open to learners from around the world and was free of charge to join. Over the course of the week 132 participants registered from 13 countries.

This unique learning opportunity was designed to prepare participants to handle and analyze multiple data types in hopes that their own research may benefit from collaborative, multi-modal approaches. Critically, participants also learned about best practices for data management and quality control in the context of integrative analysis. Speakers represented a cross-section of KCNI leadership and members of laboratory teams.

KCNI OPEN HOUSE

On June 27, KCNI hosted its fourth annual Open House, welcoming approximately 120 attendees both in-person and virtually. The energy level was high this year as the focus of the event was on the work of KCNI trainees, showcasing the young talented scientists advancing neuroinformatics. Each Lab had a designated zone of the offices where trainees showcased their poster presentations. This year conference travel has really picked back up so many trainees had the opportunity to showcase their posters from recent conferences as well as practice for upcoming ones. This year the theme was growth. Next year, KCNI will take a look back at the first full five years of the centre.



KREMBIL CENTRE FOR NEUROINFORMATICS SPEAKER SERIES

The KCNI's monthly Speaker Series is designed to highlight research topics, share knowledge and spark conversation among leading scientists and research institutions worldwide in the field of neuroinformatics, computational neuroscience and psychiatry.

The series features speakers from a wide range of backgrounds, expressing the diversity of the Krembil Centre's scientific breadth. Each month KCNI scientists offer a new perspective on the current state of multi-scale neuroscience, from gene to circuits, from brain dynamics to cognitive modeling and populations.

Presenters and topics over the past year included:

Dr. Liisa Galea, Why Sex and Sex Hormones Matter for Neuroscience of Mental Health

Dr. Gillian Strudwick, Utilization of digital innovation in mental health research: Case Studies in Mental health Research

Dr. Jed Meltzer, The role of interhemispheric interactions in neurological disorders, and what to do about it.

Dr. Sarah Gooday, Participant-centered digital health research using wearables and smartphones - Empowering the patient to co-navigate their mental health experiences and exploration of potential new states of health

Dr. Gerold Schmitt-Ulms, From protein function to therapy: targeting sodium-potassium pumps for the treatment of prion diseases and Alzheimer's disease

Dr. Kelly Smart, Molecular imaging of synaptic processes in human brain function

Dr. Bengi Baran, Understanding the role of sleep oscillations in symptoms and cognitive deficits in psychotic disorders.

Dr. Ryan Smith, Simulating the Computational Mechanisms of Emotional Awareness and their Breakdown in Affective Disorders.

Dr. Angela Laird, Large, open datasets for human connectomics research: Considerations for reproducible and responsible data use

Dr. Jesse Gillis, Generalizable cell-type markers for neuroscience

Dr. Philipp Sterzer, Predictions, perception, and psychosis

"Building a strong and innovative research community includes encouraging diverse expertise, cross-knowledge sharing and collaborative innovation across all scientists. KCNI's Speaker Series showcases the real contributions experiences by recognize scientists around the world. Through these forums, we can inspire each other, in order to better define, prevent and treat mental illnesses."

- Cindy Khuu, *KCNI Program Manager*

THANK YOU

Thank you for your continued leadership support of the Krembil Centre for Neuroinformatics and CAMH, as we strive change mental health care forever. Your generosity is advancing research and education initiatives that are improving care for patients today, and laying the groundwork that will dramatically change care for the patients of tomorrow.

Together we are building a data-driven centre of excellence that we believe will become the global hub for collaborative innovations in mental health and addiction with organizations from around the world. We are thrilled to see what the future holds, and are grateful for your partnership.

APPENDIX - PUBLICATIONS

KCNI SCIENTIST PUBLICATIONS - OCTOBER 1, 2022 TO SEPTEMBER 30, 2023

1. Arbabi, K. et al. Investigating microglia-neuron crosstalk by characterizing microglial contamination in human and mouse patch-seq datasets. *iScience* 26, 107329 (2023)

2. Price, K. M. et al. Identification of brain cell types underlying genetic association with word reading and correlated traits. *Mol. Psychiatry* 28, 1719–1730 (2023)

3. Venkatesan, S., Chen, T., Liu, Y., Turner, E. E. & Tripathy, S. Chrna5 is a marker of acetylcholine super-responder subplate neurons with specialized expression of nicotinic modulator proteins. https://europepmc.org/article/ppr/ppr508445

4. Beaupre, L. M., Wainberg, M., Tiwari, A. K. & Zai, C. … -DERIVED AND SELF-REPORTED SLEEP PROPERTIES ACROSS UK BIOBANK PARTICIPANTS WITH LIFETIME MAJOR DEPRESSIVE DISORDER. *European*

5. Wu, R. et al. Fragmentation of rest periods, astrocyte activation, and cognitive decline in older adults with and without Alzheimer's disease. *Alzheimers*. Dement. 19, 1888–1900 (2023)

6. Ling, S., Puts, M., Sproule, B. & Cleverley, K. Experiences of patient-initiated discharge from an inpatient withdrawal management service: a qualitative descriptive study. *J. Subst. Use* 1–9

7. Beyraghi, N., Cuperfain, A. B., Ghazavi, Y., Kaduri, P. & Ling, S. Description and Initial Evaluation of a Postdischarge Intervention to Support Transition of Care in Substance Use Disorder Treatment. *Canadian Journal of Addiction* 14, 20 (2023)

8. Di Paola, F., Franchuk, S., Katz, R., Kendell, E. & Ling, S. Involuntary Hospital Admission in the Treatment of People With Severe Substance Use Disorder. Canadian *Journal of Addiction* 14, 22 (2023)

9. Maslej, M. M., Kloiber, S., Ghassemi, M., Yu, J. & Hill, S. L. Out with AI, in with the psychiatrist: a preference for human-derived clinical decision support in depression care. *Transl. Psychiatry* 13, 210 (2023)

10. Strafella, R. et al. Identifying Neurophysiological Markers of Intermittent Theta Burst Stimulation in Treatment-Resistant Depression Using Transcranial Magnetic Stimulation–Electroencephalography. *Biol. Psychiatry* 94, 454–465 (2023)

11. Sheen, J. Z. et al. Cardiovascular biomarkers of response to accelerated low frequency repetitive transcranial magnetic stimulation in major depression. *J. Affect. Disord*. 318, 167–174 (2022)

12. Griffiths, J. D., Shen, K. & Gleeson, P. *Neuroinformatics of Large Scale Brain Modelling*. (Frontiers Media SA, 2022).

13. Strudwick, G. et al. Utilizing an Informatics Engagement Strategy as an Approach to Sustain and Retain the Nursing Workforce. *Nurs. Leadersh*. 35, 42–54 (2023)

14. Racey, M. et al. Technology-Supported Integrated Care Innovations to Support Diabetes and Mental Health Care: Scoping Review. *JMIR Diabetes* 8, e44652 (2023)

15. Sikstrom, L. et al. Predictive care: a protocol for a computational ethnographic approach to building fair models of inpatient violence in emergency psychiatry. *BMJ Open* 13, e069255 (2023)

16. Strudwick, G. People taking control of their own health information. *Clinics in Integrated Care* 17, 100140 (2023)

17. Gatov, E., Strudwick, G., Wiljer, D. & Kurdyak, P. E-Mental Health Services in Canada: Can They Close the Access Gap? *Healthc. Policy* 19, 40–48 (2023)

18. Strudwick, G. Commentary: A systematic review of informatics competencies: requirements for nurse managers in healthcare organisations. *J. Res. Nurs*. 28, 312–313 (2023)

19. Gur, R. E. & Gur, R. C. Functional magnetic resonance imaging in schizophrenia. *Dialogues Clin. Neurosci.* 12, 333–343 (2010)

20. Banaj, N. et al. Cortical morphology in patients with the deficit and non-deficit syndrome of schizophrenia: a worldwide meta- and mega-analyses. *Mol. Psychiatry* (2023) doi:10.1038/s41380-023-02221-w

21. Poline, J.-B. et al. Data and Tools Integration in the Canadian Open Neuroscience Platform. *Sci Data* 10, 189 (2023)

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23. Calarco, N. et al. Multivariate Associations Among White Matter, Neurocognition, and Social Cognition Across Individuals With Schizophrenia Spectrum Disorders and Healthy Controls. *Schizophr. Bull*. (2023) doi:10.1093/schbul/sbac216

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26. Mazza, F., Guet-McCreight, A., Valiante, T. A., Griffiths, J. D. & Hay, E. In-silico EEG biomarkers of reduced inhibition in human cortical microcircuits in depression. *PLoS Comput. Biol.* 19, e1010986 (2023)

27. Howard, D. et al. An in vitro whole-cell electrophysiology dataset of human cortical neurons. *Gigascience* 11, (2022)

28. Kharaghani, A. et al. Association of Whole-Person Eigen-Polygenic Risk Scores with Alzheimer's Disease. *bioRxiv* 2022.09.13.507735 (2022) doi:10.1101/2022.09.13.507735

29. Abdelhack, M. et al. Sleep-insomnia superposition: opposing brain signatures of sleep in task-based and resting-state conditions. *bioRxiv* 2023.05.13.540646 (2023) doi:10.1101/2023.05.13.540646

30. Chen, Y. et al. Robust differences in cortical cell type proportions across healthy human aging inferred through cross-dataset transcriptome analyses. *Neurobiol. Aging* 125, 49–61 (2023)

31. Kerrebijn, I. et al. Case-control virtual histology elucidates cell types associated with cortical thickness differences in Alzheimer's disease. *Neuroimage* 276, 120177 (2023)

32. Saperia, S. et al. Modeling effort-based decision making: Individual differences in schizophrenia and major depressive disorder. *Biol. Psychiatry Cogn. Neurosci. Neuroimaging* (2023) doi:10.1016/j.bpsc.2023.05.009

33. Abdelhack, M. et al. A Modulation Layer to Increase Neural Network Robustness Against Data Quality Issues. *arXiv* [cs.LG] (2021)

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36. Tio, E. & Felsky, D. The interaction of polygenic risk for depression and age on white blood cell count. *bioRxiv* (2022) doi:10.1101/2022.11.20.22282570

37. Melhuish Beaupre, L. M. et al. Association analyses of the autosomal genome and mitochondrial DNA with accelerometry-derived sleep parameters in depressed UK biobank subjects. *J. Psychiatr. Res*. 157, 152–161 (2023)

38. Yang, M. et al. Multi-omic integration via similarity network fusion to detect molecular subtypes of ageing. *Brain Commun* 5, fcad110 (2023)

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40. Derome, M. et al. Functional connectivity and glutamate levels of the medial prefrontal cortex in schizotypy are related to sensory amplification in a probabilistic reasoning task. *Neuroimage* 278, 120280 (2023)

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46. Karvelis, P., Paulus, M. P. & Diaconescu, A. O. Individual differences in computational psychiatry: A review of current challenges. Neurosci. Biobehav. Rev. 148, 105137 (2023)

47. Charlton, C. E. et al. Atypical prediction error learning is associated with prodromal symptoms in individuals at clinical high risk for psychosis. *Schizophrenia* (Heidelb) 8, 105 (2022)

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APPENDIX - AWARDED GRANTS

AWARDED GRANT APPLICATIONS - OCTOBER 1, 2022 TO SEPTEMBER 30, 2023

PI	In Collaboration With	Organization/Grant Opportunity Title	Grant Title	Notice Date of Decision	$ KCNI PIs
Andreea Diaconescu/ Etay Hay	Hay & Kiang	Miner's Lamp Innovation Fund	Improving early diagnosis of schizophrenia using cell-specific EEG biomarkers	21-Mar-2023	$20,000
Erin Dickie	Brainhack Toronto	OBI Event Funding	BrainHack Toronto	11-Nov-2022	$3,500
Erin Dickie	Anil Malhotra (ZHH), Voineskos, Lencz, Hawco	Welcome Trust	Using rTMS to Enhance Social Cognition in People with Psychosis		$20,000
Etay Hay	Tarek Rajji, Heather Brooks	UofT Labatt Catalyst Fund	Linking depression with cognitive impairment in ageing using EEG biomarkers of cortical microcircuit inhibition	29-Oct-2022	$77,000
John Griffiths	B. Zrenner, J. D. Griffiths, C. Zrenner,	CIHR	Theta-Oscillation Activity Synchronized TMS of the DMPFC: A Precision Medicine Treatment for OCD (TOAST-OCD)		$140,000
Laura Sikstrom	S Hill, M Maslej	Google Award for Inclusion Research	A Computational Ethnographic Approach to Building Fair Models of Inpatient Violence in Emergency Psychiatry	17-Oct-2022	$82,377
Laura Sikstrom	Darla Reslan	Critical Data Humanities Intitiative Fellowship Program	When measures become targets: unintended consequences of psychiatric AI	1-Dec-2022	$3,500
Laura Sikstrom	A Amaral, M Chapman, A Martel, M Goubran, P Maralani, M Burke, F Pirouzmand, E McLellan	Kimel-Schatzky TBI Research and Innovation Fund	Improving the experience of family members of traumatic brain injury (TBI) patients using iterative predictive models for long term functional outcomes.	18-Jan-2023	$40,000
Laura Sikstrom	M. Maslej, Valeria Khudiakova	T-Cairem Summer Studentship	Building Fair Machine Learning Models: Using Big Data to Predict Risk of Aggression in Autistic ED Patients at the Centre for Addiction and Mental Health	5-Apr-2023	$3,600

PI	In Collaboration With	Organization/Grant Opportunity Title	Grant Title	Notice Date of Decision	$ KCNI PIs
Marta Maslej	L. Sikstrom, S. Hill	Google Award for Inclusion Research	A Computational Ethnographic Approach to Building Fair Models of Inpatient Violence in Emergency Psychiatry	17-Oct-2022	$82,377
Marta Maslej	Laura Sikstrom, Valeria Khudiakova	T-Cairem Summer Studentship	Predicting Risk of Aggression in Autistic ED Patients at the Centre for Addiction and Mental Health		$3,500

Centre for Addiction and Mental Health Foundation
100 Stokes Street, 5th floor, Bell Gateway Building
Toronto, Ontario Canada M6J 1H4

camh.ca

Charitable Registration Number: 106932320RR0001

camh
FOUNDATION

	Actuals						Actuals/Forecast
	Year 6 Cumulative 2022/23	Year 7 2023/24	Year 8 2024/25	Year 9 2025/26	Year 10 2026/27	Year 11 2027/28	Total
REVENUE							
Krembil Funding	$ 10,261,732	$ 1,343,365	$ 1,054,466	$ 1,042,375	$ 1,066,148	$ 268,033	$ 15,036,119
Krembil AI Funding	$ 435,600	$ 684,779	$ 475,598	$ 492,577	$ 250,608	$ -	$ 2,339,161
Krembil Funding Phase 2- New Funding $12.5M	$ 631,313	$ 2,840,909	$ 2,777,778	$ 2,777,778	$ 2,777,778	$ 694,445	$ 12,500,000
Foundation AI Funding	$ 140,000	$ 140,000	$ 140,000	$ 140,000	$ 140,000	$ 700,000	$ 1,400,000
(BHDB) Discovery Fund	$ 5,872,273	$ 1,007,236	$ 620,492	$ -	$ -	$ -	$ 7,500,000
Koerner/Other	$ 1,347,540	$ -	$ -	$ -	$ -	$ -	$ 1,347,540
Sankey/Pearson	$ 60,000	$ 45,000	$ 35,000	$ 25,000	$ 10,000	$ -	$ 175,000
Keystone/Meekison	$ -	$ 100,000	$ 100,000	$ 100,000	$ 100,000	$ 100,000	$ 500,000
Other Foundation Grants	$ 7,279,813	$ 1,152,236	$ 755,492	$ 125,000	$ 110,000	$ 100,000	$ 9,522,540
COVID-19 Funding	$ 1,232,406	$ -	$ -	$ -	$ -	$ -	$ 1,232,406
CAMH Contribution	$ 4,491,116	$ 693,768	$ 714,581	$ 736,019	$ 758,099	$ 780,842	$ 8,174,425
TOTAL REVENUE	**$ 24,471,980**	**$ 6,855,057**	**$ 5,917,914**	**$ 5,313,748**	**$ 5,102,632**	**$ 2,543,320**	**$ 50,204,651**
CENTRE EXPENSES							
Core Centre Team	$ 3,429,092	$ 889,496	$ 916,181	$ 943,666	$ 971,976	$ 1,001,154	$ 8,151,565
Scientific Director Start-Up + Seed	$ -	$ 200,000	$ 200,000	$ 200,000	$ -	$ -	$ 600,000
Technical Team	$ 446,994	$ 60,000	$ 534,000	$ 818,230	$ 842,777	$ 259,893	$ 2,961,894
BrainHealth Databank	$ 5,872,273	$ 1,007,236	$ 620,492	$ -	$ -	$ -	$ 7,500,000
KCNI Scientists	$ 5,975,169	$ 1,796,658	$ 1,072,511	$ 772,500	$ 795,675	$ 819,545	$ 11,232,058
KM Scientist + Project Costs	$ -	$ -	$ 504,000	$ 519,120	$ 534,694	$ 550,734	$ 2,108,548
AI Scientist + Project Costs	$ 691,851	$ 679,779	$ 702,944	$ 726,650	$ 751,160	$ 776,501	$ 4,328,885
KTE & Communications	$ 88,266	$ 52,000	$ 52,000	$ 52,000	$ 52,000	$ 52,000	$ 348,266
Infrastracture/Capital	$ 2,100,179	$ -	$ -	$ -	$ -	$ -	$ 2,100,179
Shared Research Infrastructure Fund	$ 848,532	$ 344,385	$ 321,929	$ 285,490	$ 236,173	$ 57,444	$ 2,093,954
Foundation General Fund	$ 480,377	$ 21,500	$ 20,500	$ 19,500	$ 18,000	$ 45,000	$ 604,877
CAMH In-kind	$ 4,491,116	$ 693,768	$ 714,581	$ 736,019	$ 758,099	$ 780,842	$ 8,174,425
TOTAL CENTRE EXPENSES	**$ 24,423,849**	**$ 5,744,822**	**$ 5,659,138**	**$ 5,073,176**	**$ 4,960,554**	**$ 4,343,113**	**$ 50,204,651**
SURPLUS/(DEFICIT)	**$ 48,131**	**$ 1,110,235**	**$ 258,776**	**$ 240,573**	**$ 142,078**	**$ (1,799,793)**	**$ -**
CUMULATIVE SURPLUS/(DEFICIT)		**$ 1,158,366**	**$ 1,417,142**	**$ 1,657,715**	**$ 1,799,793**	**$ -**	