camh | Krembil Centre for Neuroinformatics

Impact Report

Krembil Centre for Neuroinformatics

From Neuronal to National: Scaling Innovation in Mental Health Research and Care

October 2022

A Message from
the Directors

Thank you for your support of the Krembil Centre for Neuroinformatics and the important role you are playing in building awareness about mental illness and addiction, both here in Toronto and around the world. Together, we are revolutionizing how big data can be applied to predict and diagnose mental illness sooner and ensure people receive care that is tailored to the individual and their family.

We are proud of the tremendous team of brilliant and compassionate researchers we have recruited, who are driven to advance care for people who rely on us. As you will read in this report, 2021-2022 included significant leaps in clinical care, headline-generating discoveries, one-of-a-kind educational opportunities, and a welcome return to in-person connections with our communities. All made possible by our partnership with you.

Our unparalleled foundation of discovery and knowledge has quickly elevated the Krembil Centre as a national leader in brain sciences. This led directly to the October 7 announcement made by Brain Canada that CAMH will lead the development of the Canadian Youth Mental Health Insight Platform (CYMHI), the largest youth mental health data platform to mobilize knowledge worldwide.

This state-of-the-art informatics tool will use open data, machine learning and online interfaces to optimize mental health for youth across Canada. A truly national collaborative effort, this three-year project will involve youth, family, service providers, policymakers, and health and data scientists from coast to coast to coast.

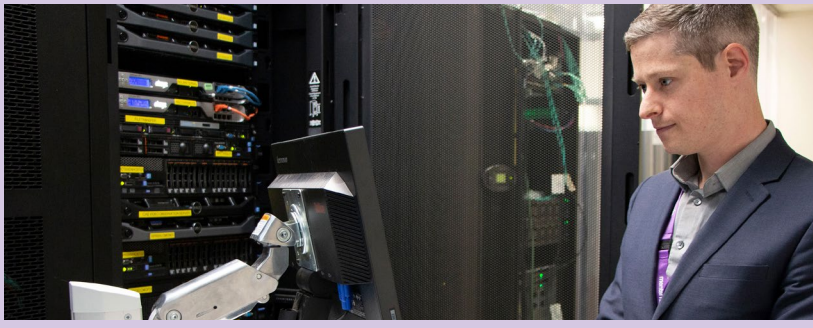
We are delighted to share in this landmark accomplishment with you, as it couldn't have happened without your support.

In closing, what's truly remarkable to us is that we feel like we are only scratching the surface of what is possible. With the restrictions of the pandemic slowly lifting, there is renewed energy in the air. We hear it in our labs, in the common areas, and at our events. Spaces are coming alive again, spurring on new collaborations and ideas. People are excited to show the world what we can really do.

Thank you for your steadfast faith in our vision to revolutionize brain research and improve mental health care, for everyone.

Dr. Sean Hill
Scientific Director,
Krembil Centre for Neuroinformatics

Dr. David Rotenberg
Operations Director,
Krembil Centre for Neuroinformatics



Krembil Centre for Neuroinformatics

2021-2022 By the Numbers

80 Total Team Members Including **+2** new team members

56 Trainees Including **+4** new trainees

42 Trainees Graduated **+17** more graduates than 2021

84 Events/Conference Speaking Engagements

103 Publications **+49** increase from 2021

71 Grants Awarded **+31** compared to 2021

$4,864,619 Grants Awarded Revenue (KCNI)

Canadian Youth Mental Health Insights Platform

CAMH to create groundbreaking youth mental health data platform

Knowledge exchange initiative to improve quality of research and care for young people Canada-wide

On October 7, CAMH, in collaboration with youth, family, service providers, policymakers, as well as health researchers and data scientists from across Canada, announced it will build the Canadian Youth Mental Health Insight Platform (CYMHI), powered by RBC Future Launch, with support from Power Corporation, and the Canada Brain Research Fund (CBRF). This 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.

> The state-of-the-art informatics tool will incorporate information from diverse organizations across the country including academic institutions, community-based mental health services, hospitals, and youth and family advisories from organizations such as Foundry, Youth Wellness Hubs Ontario and other youth substance use and mental health services. The CYMHI platform will facilitate high-impact research and the development of innovative youth mental health approaches that would otherwise not be possible."
>
> **Dr. Sean Hill, Director of the Krembil Centre of Neuroinformatics, and principal investigator**

CAMH leads the pan-Canadian team that has been 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. The Krembil Foundation's leadership support of the Krembil Centre of Neuroinformatics played an integral role in securing this funding.

> We know that many youth in Canada are in crisis. Young people are experiencing mental health challenges now more than ever, but there are so many barriers to care: lack of local services, lack of access to the best treatments, and lack of cohesion among experts working to solve these problems. The CYMHI will address these problems by connecting youth, families, researchers, policymakers and community organizations to improve services and programming for youth across the country."
>
> **Dr. Joanna Henderson, Director of CAMH's Margaret and Wallace McCain Centre for Child, Youth & Family Mental Health, and project co-lead**

The platform will enable knowledge sharing in creative new ways. One feature will be personalized services tool to match youth based on their unique needs to available services in their area. It will include precision modelling to predict the future needs of individual youth and help them and their families make decisions about their care. And, it will also incorporate a national atlas of service demand and utilization—the largest of its kind ever built—to help decision-makers understand a community's youth mental health needs in order to better allocate resources.

To hear from the leaders of this project, click here.

> In high school I tried to end my life three times before I was finally able to access help. And even then, I had to travel six hours away from home to get the treatment I needed to be healthy. The CYMHI platform will help ensure that young people across the country have access to the best practices and evidence-informed treatments no matter where they live. This will allow youth to have informed consent of their treatment options and make decisions for their care that fit their needs best. CAMH is also building young people's voices and concerns into the DNA of this project. It's making knowledge accessible to everyone, not just a privileged few, removing the silos and gate keeping in the youth mental health sector."

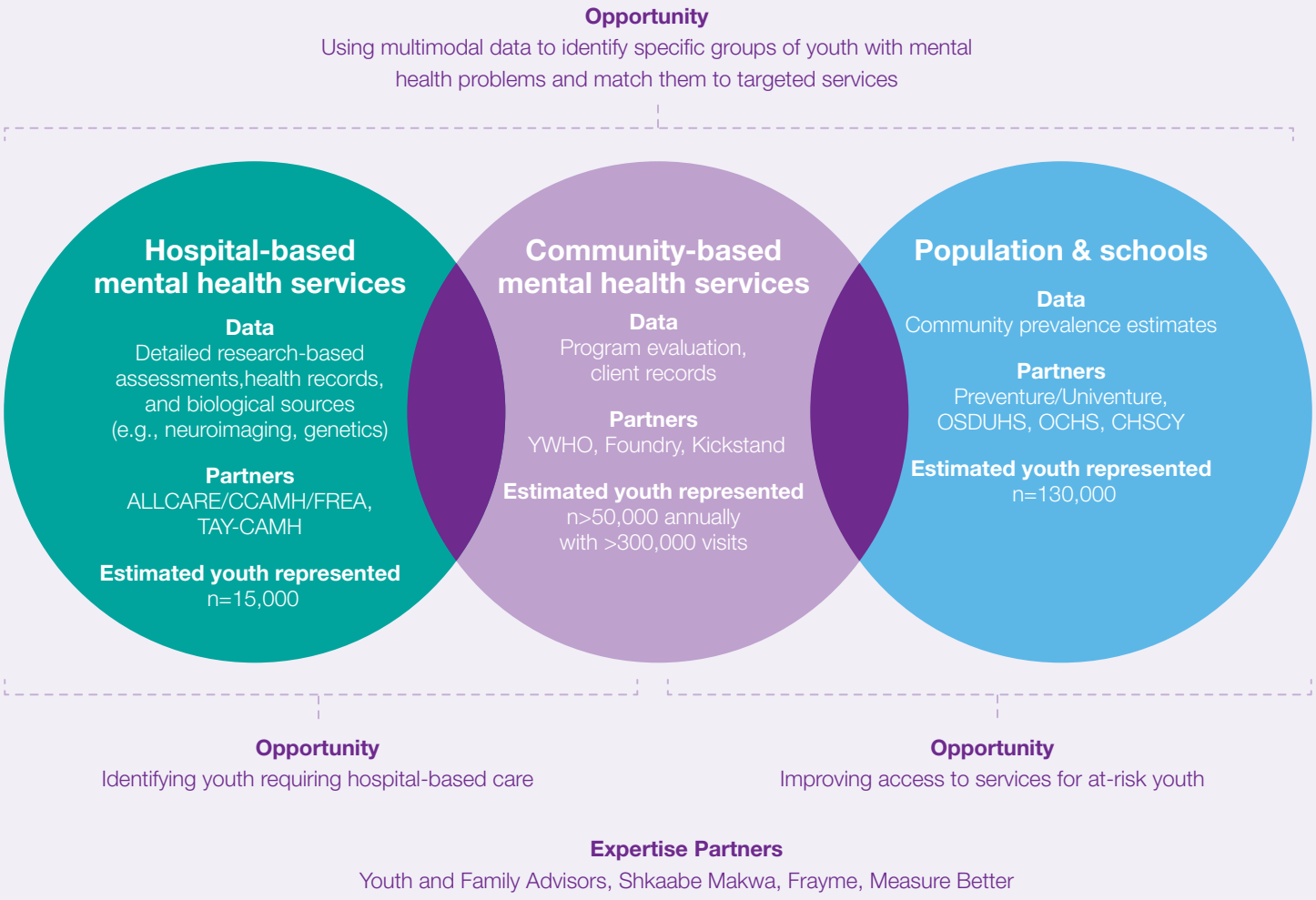
Cierra Garrow, an advisor on the project with first-hand experience of trying to navigate the youth mental health system

Click below to view media coverage of the Brain Canada announcement

Toronto Star

The Globe and Mail

Global News



BrainHealth Databank

Now in its fourth 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 Dr. Arturo Santisteban[1], has collaborated with stakeholders from across CAMH, including the Research Office, CAMH researchers, patient and family advisors, and Research Executive Committee, to draft policy and standard operating procedures relating to the collection, storage, and use of data, with a significant focus on privacy and harmonization. Once complete, these policies and procedures will be sustainably instituted at the organizational level and embedded across CAMH. The BrainHealth Databank team is striving for governance policy approval from CAMH's Research Committee by the end of the 2022.

Innovative decision support tools go live for clinicians and patients

Measurement-based care makes it possible to collect, streamline and leverage patient information to enhance clinical decision-making and the overall patient experience in a meaningful and tangible way. While measurement-based care has been a standard in the management of ongoing physical health conditions, it has been underutilized in mental health care. To address this, the BrainHealth Databank implemented patient-level decision support tools for clinicians to support measurement-based care, as well as patient-facing dashboards where they can see their treatment course over time.

This model equips healthcare providers with additional tools and information that support clinical decision-making and helps synthesize data related to the client's treatment trajectory based on various data points. Patients also benefit from this transparent model by being empowered to take a more active approach in their care.

65+

CAMH Stakeholders

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

7

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

10

Collaborative Awards
Including grants and fellowships

12

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

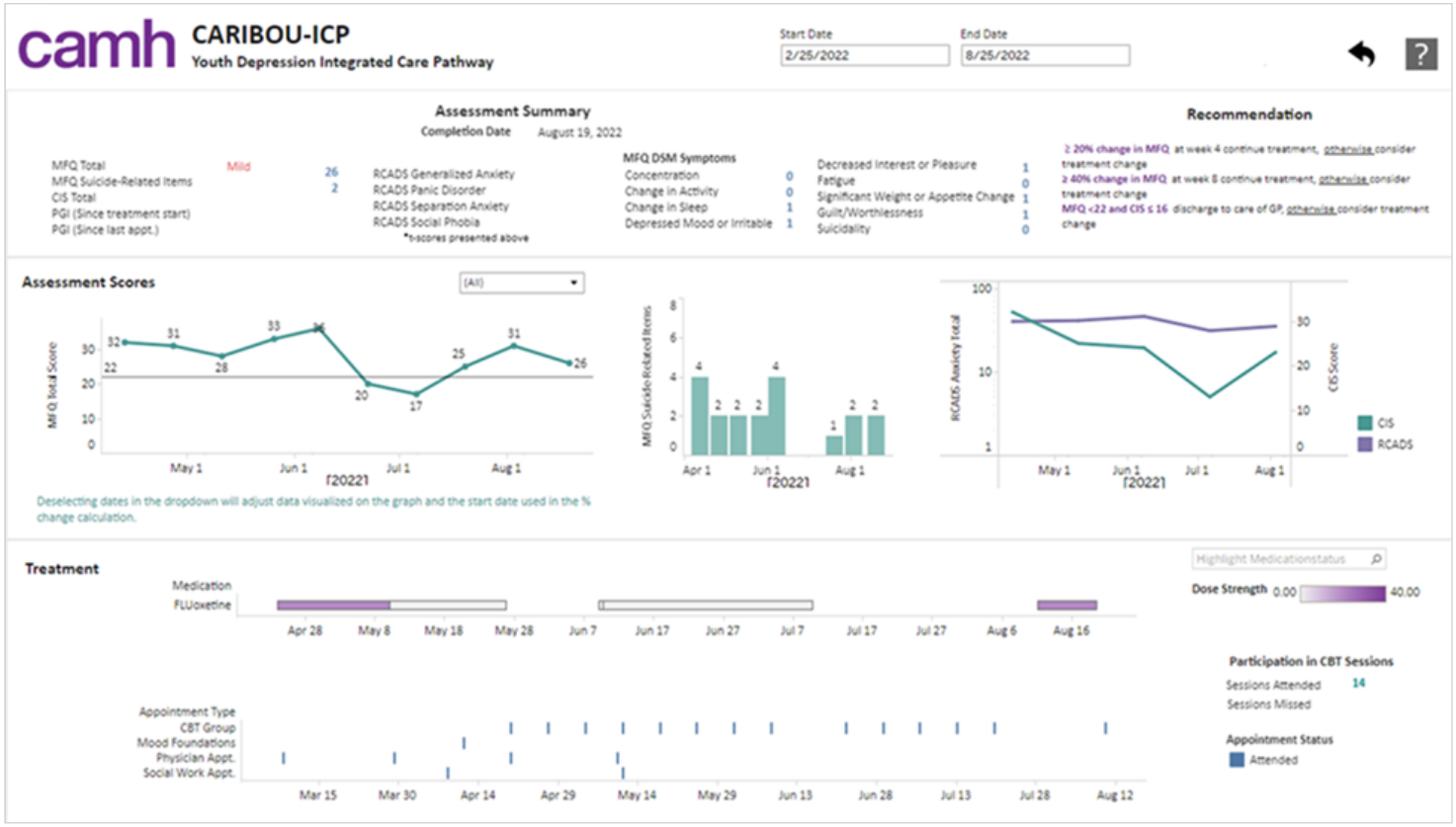
Visit the new BrainHealth Databank website

1 Dr. Joanna Yu is on maternity leave until late-2022.

Benefitting clinics across CAMH

There are currently three decision support tools implemented and in use for CAMH clinical programs, including Ontario Structured Psychotherapy, Care for Adolescents who Receive Information 'Bout OUtcomes (CARIBOU) Integrated Care Pathway and Major Depressive Disorder Integrated Care Pathway (MDD-ICP). These tools have been well-received by clinicians and patients alike. There are currently three more in development and requests for an additional 10.

The decision support tool is at the heart of a culture shift embodied in CAMH's strategic plan, **One CAMH**, where all stakeholders—from clinicians to researchers to patients and families—are part of a hospital-wide collaborative effort to enhance patient-centred measurement-based care. The dashboard was made possible by collaboration across multiple CAMH teams, including: Clinical Applications, Data Strategy & Business Intelligence, Research IT/KCNI, and physician and patient-partner groups.



Looking ahead

The work does not stop with creating these decision support tools. As part of the BrainHealth Databank's commitment to sustainability and continuous engagement, they will be routinely engaging clinical champions to provide feedback on how to further improve and build awareness of this technology so that additional pathways can be developed that will allow these dashboards to be expanded moving forward.

The patient dashboards will support measurement based care at CAMH

19 Digital Measurement-Based Care Pathways

Implemented Across **7** Clinics

11,443 Enrolled Patients

Seen by **152** Clinicians

5,787,410 Data Points

What clinicians are saying:

"As part of the CARIBOU pathway, these decision support tools present a fantastic opportunity to enhance shared decision making with youth around the treatment of depression. The visualizations help convert complex information to an accessible format that can be used as a springboard for discussion at clinical appointments. We are so grateful for the support of the BrainHealth Databank towards the development of these valuable new tools."

Darren Courtney, Clinician Scientist in the Concurrent Youth Unit

"The decision support tool of the MDD-ICP enables a one-page visualization and overview of the most important clinical aspects of patients' care trajectories for the clinic team. This would be impossible using common medical records. Sharing this information with patients empowers them to assume an active and informed role in decisions about their care."

Dr. Stefan Kloiber, Clinician Scientist and Medical Head in the General and Health Systems Psychiatry Division

"The patient-level dashboards provide a wealth of important information that staff can use to monitor progress and enhance clinical decision making regarding a client's treatment plan. Clients have also appreciated being able to see graphs of how their symptoms have changed, which positively reinforces the significant efforts they are making to improve their mental health."

Dr. Judith Laposa, Psychologist and Clinician, Scientist in the Mood and Anxiety Service, CAMH, Clinical and Training Lead for the Ontario Structured, Psychotherapy Program

Using data to understand how mental health symptoms develop in youth

The BrainHealth Databank is playing a vital role in the collection and management of data and biosamples for the Toronto Adolescent & Youth (TAY) Cohort Study. The TAY Cohort Study aims to better understand how certain symptoms of mental illness can develop, who is at an increased likelihood of developing certain mental health challenges, and how we can better support young people. Funded by the CAMH Discovery Fund for a period of six years, this groundbreaking longitudinal cohort study will follow 3,000 youth ages 11-24, who are currently accessing mental health services within the Child, Youth, and Emerging Adult Program at CAMH. Over the course of the study, each participant has the opportunity to participate in different activities that look at biological (i.e., brain structure, heart rhythms), clinical, cognitive, social and family-based data. This information will be used to build a thorough, multi-scale picture of the whole individual from genes to brain, behaviour and community.

232
biosamples including
64
microarrays, managed through the Biobank and LabKey

289
participants assessed clinically through REDCap

169
MRI sessions managed through XNAT

171
Respiratory Sinus Arrythmias stored as time series data

Opening a digital front door for patients

A priority of CAMH is the re-imagination of the patient journey using scalable technologies like mobile apps, wearables, etc., to support patients at the times and places that work for them. CAMH has integrated many digital products that support and improve the patient journey; however, they are not well connected in a way that presents as one unified front-end to patients. It is vital for these inputs to be aligned to ensure patient-centred 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. 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. The platform will align with measurement-based care as well as virtual care, and include features seen in traditional patient portals.

To deliver this single point of entry and seamless experience for CAMH clients, the Digital Front Door will build foundational infrastructure to integrate disparate tools on the back-end, connecting new and existing technologies within the CAMH ecosystem. The product will have architecture to allow for curation of content and tools that meet the needs of patients and families while supporting clinical workflows now and over the long-term. Over time, as the platform becomes integrated into clinical workflows, clinicians will be able to "plug and play" modules for patients, providing a truly customized digital care plan and ensuring continuous quality improvement. A request for proposals for a technology partner closed in September.

"Patient inputs are being taken seriously at BrainHealth Databank while the encouragement that was given to actively participate at all levels is nothing less than inspiring. I would like to extend my heartfelt gratitude to the whole BrainHealth Databank team for having taken such positive steps towards putting patients and families at the core of everything they do."

Rohan Mehta, Patient Advisory Committee

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. Phase two will build upon and leverage the first phase of the BrainHealth Databank to accomplish the following:

- **Extend** the BrainHealth Databank beyond the walls of the CAMH;
- **Deploy** digital measurement-based care and scalable decision support tools;
- **Expand** wearable services and actigraphy for sleep measures across the hospital;
- **Enhance** AI pipelines for personalized care and pilot implementation in clinics;
- **Become** world leaders in Open Science in mental health; and
- **Advance** national and international collaborations.

To achieve these goals, the BrainHealth Databank will be a key stakeholder in the IntegralHealth Platform, which will implement the federation of clinical and research data across Toronto, Ontario, and Canada.

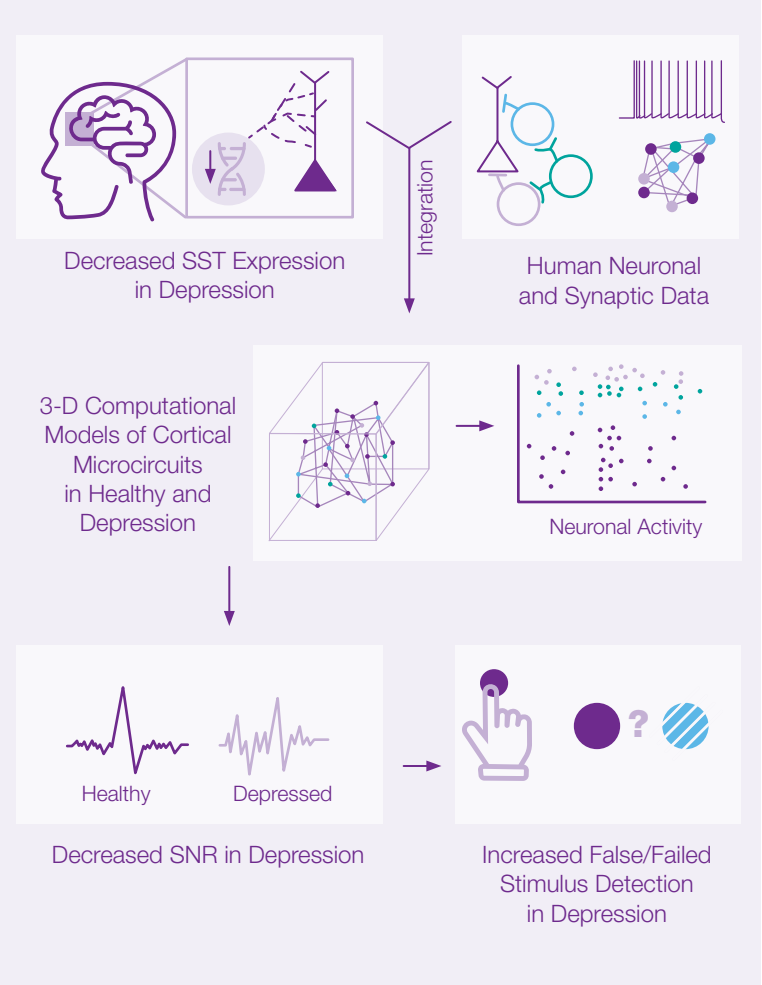
Significant Breakthroughs and Publications

1. Building a better model of brain neuronal networks

The rise of neuroinformatics has allowed us to build the most sophisticated simulations ever of human neurons and the networks of the brain; however, to date researchers have not been able to study experimentally how the neurons interact in a living brain. Thanks to a unique partnership between the Krembil Centre for Neuroinformatics and the Krembil Brain Institute at UHN, CAMH scientists have created the world's first model of human brain microcircuitry in health and depression that incorporates the properties of live human brain cells and gene expression post-mortem data from depression patients.

Led by Dr. Etay Hay, Independent Scientist at the Krembil Centre for Neuroinformatics, the team sought to use computer models based on live human brain tissue to confirm a hypothesis about what depression looks like in the brain. Among the first results from this partnership is a CAMH led study entitled, "Reduced inhibition in depression impairs stimulus processing in human cortical microcircuits," recently published in the leading journal *Cell Reports*. In the paper, the authors demonstrated how a type of treatment resistant depression manifests itself in the brain, specifically linking the role of a particular type of neuron known as Somatostatin (SST) to impaired cognitive function.

The living brain cells used in this model came from healthy brain tissue extracted during surgery in epilepsy patients. The authors believe this new simulation of the human brain integrating data from living brain cells may have enormous implications for future research at CAMH and around the world, and could pave the way for a new generation of drugs for treatment resistant depression.



"Incorporating what we've learned from living brain tissue, our new model allows us to better predict how different types of conditions will affect real functioning brain cell networks. This is brand new and the potential for what we can learn using this model is very exciting."

Dr. Etay Hay, Independent Scientist at the Krembil Centre for Neuroinformatics

The team is already using the new model to simulate the effect of the SST neuron on EEG brain signals, so that they can eventually diagnose this in patients. In another study, they are testing new compounds like the ones Dr. Etienne Sibille, Senior Scientist and Campbell Family Chair in Clinical Neuroscience, has developed in his work on reversing memory loss, to demonstrate their real-world impact on the brain. Testing these treatments on the realistic computer model is the next step towards eventual human trials, and expediting treatments.

2. Mental illness associated with poor sleep quality according to largest study of its kind

People who have been diagnosed with a mental illness are more likely to have poor sleep quality compared to the general population, according to the largest study of its kind ever conducted. The study, "Accelerometer-derived sleep measures and lifetime psychiatric diagnoses," led by researchers at the Krembil Centre for Neuroinformatics, was published in the journal *PLOS Medicine* in October 2021 and received international coverage.

Researchers found that the relationship between sleep and mental health was bi-directional: poor sleep contributes to poor mental health and poor mental health contributes to poor sleep. Sleep pattern differences were a feature of all mental illnesses the team studied, regardless of diagnosis.

"The differences in sleep patterns indicated worse sleep quality for participants with a previous diagnosis of mental illness, including waking up more often and for longer periods of time. Until now nobody has looked at objectively measured sleep in the context of mental illness at quite this scale. Part of why we wanted to do this study is that with the emergence of smartphones and wearables, we have access to data streams that we never had before."

Senior author Dr. Shreejoy Tripathy, Independent Scientist at CAMH's Krembil Centre for Neuroinformatics.

The study was based on data collected from 89,205 participants in the United Kingdom who agreed to wear an accelerometer on their wrist that tracked body movement 24 hours a day for seven days. Their data was stored in a digital biobank. The authors used computational algorithms—including machine learning—to summarize this vast amount of data into 10 metrics, including bedtime, wake time, naps and the longest duration of uninterrupted sleep. They then compared these metrics between participants who had received a previous diagnosis of mental illness in their lifetime and those who had not.

This is the first large-scale transdiagnostic study of objectively measured sleep and mental health. The study's unique methodology allowed for sleep monitoring to be conducted in each participant's home sleep environment rather than in a laboratory setting.

Researchers at the Krembil Centre for Neuroinformatics' are using the BrainHealth Databank to collect similar patient data to that was used in the UK study. A core goal of the Databank is to take patient data, including the use of wearables outside of a hospital setting, to deliver improved, personalized mental health care in the present, while also accelerating future clinical research, discovery and innovation.

Selected Coverage:

Toronto Star

CTV News

Neuroscience News

3. Conceptualizing fairness in healthcare

Fairness is a core concept meant to grapple with different forms of discrimination and bias that emerge with advances in artificial intelligence like machine learning. Yet, claims to fairness in machine learning discourse are often vague and contradictory.

The response to these issues within the scientific community has been technocratic: studies either attempt to mathematically measure competing definitions of fairness and/or recommend a range of governance tools (e.g., fairness checklists or guiding principles).

To advance efforts to operationalize fairness in medicine, researchers led by Dr. Laura Sikstrom, scientist at the Krembil Centre for Neuroinformatics, and including Dr. Sean Hill, synthesized a broad range of literature in their paper, "Conceptualising fairness: three pillars for medical algorithms and health equity." The paper received May 2022's Editor's Choice award from the journal *BMJ Health & Care Informatics*.

The researchers conducted an environmental scan of English language literature about fairness from 1960 to July 31, 2021. They searched the electronic databases Medline, PubMed and Google Scholar, supplemented by additional hand searches. Data from 213 selected publications were analyzed using rapid framework analysis in two rounds: to explore previously identified issues, and then issues emerging from the analysis.

Their research identified "Three Pillars for Fairness": transparency, impartiality and inclusion. Based on this insight, the researchers proposed a multidimensional conceptual framework to guide empirical research on the operationalization of fairness in healthcare.

They determined that scholars and computational scientists alike must broaden their notions of fairness to examine normative assumptions about what it means to build a just society and who decides what is fair.

Further, the operationalization of fairness requires going beyond developing rigorous data processing procedures or deploying sophisticated techniques to detect, mitigate and eliminate bias in machine learning. Predictions can be fair and accurate and still amplify inequities

A multidimensional framework for fairness entails sustained dialogue with a range of stakeholders in the careful weighing of competing claims to fairness. It also involves proactively designing machine learning tools with and for marginalized and underserved communities. Thus, fairness is not an outcome of rigorous and thoughtful research, but the social and political process required to advance health equity.

"As a social scientist, I was skeptical about the utility of the notion of 'fairness' in the computer sciences. But conceptualizing fairness as a multidimensional social process forces us to ask bigger questions about how AI might transform care in medicine. Everyday conversations about fairness in AI are really social and political debates about how these tools are made, for whom and to what ends. I am now convinced that fairness propels values-based design and technological innovation of AI-enabled tools in medicine."

Dr. Laura Sikstrom, lead author and scientist at the Krembil Centre for Neuroinformatics

Krembil Centre for Neuroinformatics

Team Updates

Computational Genomics Team

Team Lead: Dr. Shreejoy Tripathy

Over the past year, the Computational Genomics team has expanded considerably, now encompassing a diverse team of 15 post-docs, graduate students, undergraduates, a Research Analyst and a Research Methods Specialist. Simultaneously, the team has cultivated a wide network of world-leading collaborators that span the breadth of experimental neuroscience to clinical practice. The team pursues a range of questions at the heart of fundamental neuroscience and mental illness, such as: what makes human neurons unique? How do genetic differences across people impact how neurons function? And how can we better define and treat depression using data-driven approaches?

The team is especially proud of two major projects. The first project builds on the growing collaboration with Dr. Taufik Valiante the Krembil Brain Institute at UHN to study electrical features of live neurons in the human neocortex, immediately after they have been resected during the course of routine neurosurgery. This work has resulted in two publications, including a recent collaboration with the lab of Dr. Etay Hay, to understand how age-related changes in neuron characteristics might result in altered cortical information processing. In related work recently submitted for publication, they have used data from an additional cohort of human subjects, collected by the Allen Institute for Brain Sciences in Seattle, to understand how the brain's immune system interacts with neurons and affects their electrical processing. This work is especially important as the brain's immune system is vital to understanding complex neuropsychiatric disorders, like Alzheimer's disease and schizophrenia. Lastly, the team is continuing its efforts to expand these efforts to systematically study neuron diversity in the context of the non-human primate brain, as part of a large international collaboration led by Yale University and University of Western Ontario.

Second, over the last year the team has published a number of studies using large-scale population cohorts like the UK Biobank to better understand the multimodal and multi-faceted aspects of psychiatric illness. They are using these massive datasets to pursue a diverse array of questions, like: "How is depression defined into subtypes?," "How do cannabis use and genetics interact to contribute to psychiatric experiences?," "How are psychiatric diagnoses associated with worsening of quality of life factors, such as poor sleep quality?," and "How does rare genetic variation contribute to increased burden of psychiatric illness." They are now expanding this work to understand how genetics can provide clues into finding new drug treatments for psychiatric disorders. One exciting aspect of this work is that they are beginning to leverage these discoveries in the context of impacting and improving care pathways directly in the clinic at CAMH.

In the coming year, the team looks forward to continuing to return on-site following the difficult pandemic and the challenges of working collaboratively from home. They look forward to more opportunities to interact with our bright research collaborators and talented clinical colleagues.

Dr. Etay Hay

Brain Circuit Modelling Team

Team Lead: Dr. Etay Hay

The Brain Circuit Modelling team has successfully transferred two members from Masters to PhD programs, and another will be defending her Master's thesis in the upcoming months. A postdoctoral fellow on the team received a competitive award and an undergraduate member received a competitive summer award to continue his research. 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, in collaboration with Dr. Etienne Sibille and Dr. Shreejoy Tripathy at CAMH and Dr. Taufik Valiante at UHN, published a paper in *Cell Reports*. Their research characterized the implications of reduced inhibition on cortical processing in depression, using first-of-a-kind detailed computational models of cortical microcircuits constrained with a variety of human neuronal, synaptic and gene-expression data. The paper was published open-access, and the team has shared the models and code openly with the scientific and general community.

The team also recently published a paper in *Cerebral Cortex*, reporting for the first time changes in neuronal electrical properties that occur as we age. This work, in collaboration with Dr. Valiante and Dr. Tripathy, found changes in neuronal integration of inputs in neurons from older subjects, and used detailed computational models to show that these changes can explain the dampening of brain activity at rest in aging.

The team has added to their in-silico EEG biomarkers of altered inhibition in depression, and the work is still in peer-review. In the meantime, the team started a new project that will test these biomarkers on patient EEG data to improve patient stratification and treatment prediction.

The Brain Circuit Modelling team has also finished a collaborative project that applied the computational platform to test new CAMH-developed pharmacology on human microcircuits and cortical processing in-silico, and thus support translation of the drug clinical use. The team is currently compiling these results into a publication.

Finally, the team is completing another project in collaboration with Dr. Andreea Diaconescu that adapted the detailed models of human microcircuits to study the inhibitory changes underlying deficits of cortical microcircuit processing in schizophrenia, with the aim of refining biomarkers for diagnosis and establish candidate targets for treatment.

Whole Brain Modelling Team

Team Lead: Dr. John Griffiths

The Whole-Brain Modelling team at the Krembil Centre has moved forward on its research program agenda in several important ways during the 2021-2022 academic year. The big picture of their work is to develop and deploy mathematical models of large-scale brain network dynamics to better understand macro-scale brain activity measurements, particularly those typically used in human neuroimaging, such as EEG, MEG, fMRI, fNIRS, etc. The team uses these models to study how brains are affected by psychiatric and neurological illness, and also the mechanisms of action of therapeutic solutions such as drugs and, in particular, brain stimulation (TMS, TDCS, TACS, FUS, DBS, etc.).

One exciting technical advance, spearheaded by Dr. Zheng Wang, mathematics and analytics specialist, is a new methodology for running brain simulations within computational environments developed and optimized for modern deep learning applications. This approach has been communicated in two publications currently under review, one focusing on resting-state fMRI and the other focusing on EEG evoked responses to noninvasive brain stimulation (TMS). A third project, led by MSc student Andrew Clappison, is using this technique for integrated concurrent modelling of fMRI (and/or fNIRS) and EEG—an important and advanced direction for the field. They have started the process of packaging this tool into an open-source Python library called WhoBPyT ("Whole-Brain Modelling in PyTorch"; pronounced 'Hobbit'), which has already received interest from several research groups around the world.

Other key articles from the past year include a systematic investigation of inter-subject variability in brain connectivity of candidate anatomical targets for TMS therapy for major depression, led by PhD student Shreyas Harita, and a comprehensive review on the Past, Present, and Future of whole-brain modelling with PhD student Sorenza Bastiaens and lab alumna Dr. Neda Kaboodvand. 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 2022), International Brain Stimulation Society (IBSS 2021), Society for Functional Near Infrared Spectroscopy (SFNIRS 2022), and Canadian Neuroscience Association (CAN-ACN 2022).

Several members of the group have taken leadership roles in organizing local, national, and international scientific meetings. In December, post-doc Dr. Davide Momi and Dr. Griffiths ran a well-received symposium on brain network modelling at the IBSS 2021 conference. In May, Dr. Griffiths and several group members co-organized the 3rd annual Canadian Computational Neuroscience Spotlight (CCNS) conference; in July they supervised 10 young (undergraduate and graduate level) trainees on a week-long neuroimaging and computational modelling research project as part of the 3rd annual KCNI Summer School; and in August, three group members served as TAs during the Neuromatch Academy computational neuroscience summer school. Dr. Griffiths took leadership roles this year both internationally, as guest-editor of a special issue of Frontiers in Neuroinformatics about "Neuroinformatics of Whole-Brain Modelling" and locally, which resulted in a departmental award from the University of Toronto Institute of Medical Sciences for teaching and research excellence.

Finally, the group has continued its success in securing grant funding from competitive national competitions. This includes a new CIHR grant for closed-loop brain TMS brain stimulation for OCD (in collaboration with CAMH Temerty Centre scientists Drs. Brigitte and Christoph Zrenner), and a major CFI grant bringing important new research infrastructure to CAMH (servers and storage, mobile brain imaging systems, virtual reality devices). Several lab members have also been successful in obtaining funding for PhD scholarships, summer internships, and travel grants.

Dr. John Griffiths

Cognitive Network Modelling Team

Team Lead: Dr. Andreea Diaconescu

The Cognitive Network Modelling Group has made considerable progress towards demonstrating the utility of computational modelling in the context of suicide prevention research. Most importantly, the team has developed mathematical models of active escape biases to classify causes of emerging suicide risk in real time.

To demonstrate the clinical utility of these models, the team has established clinical partnerships within CAMH and across Toronto in the form of leadership roles on two funded grants. These projects examine the application of computational modelling for suicide prevention in at-risk individuals seeking emergency services at CAMH ($165,000, funded by CAMH Discovery Fund). The application of advanced functional magnetic resonance imaging to examine the neural basis of the identified computational mechanisms has also been supported by the Natural Sciences and Engineering Research Council (NSERC) ($130,000, funded by NSERC Discovery Grant).

The team has also pursued multiple collaborative grant applications, which focus on neurocomputational models for suicidality predictions ($100,000, funded by the American Foundation for Suicide Prevention); for clinical high risk for psychosis prediction (submitted, CIHR Project Grant); and for assessing the efficacy of psychedelic treatments (submitted, Labatt Family Innovation Fund).

To achieve their goals, the team continues to grow and now includes: one postdoctoral fellow, three Ph.D. students, two Masters students, two research analysts, and three undergraduate students, representing the fields of computational neuroscience, psychology, biomedical engineering, physics, and mathematics. The work of Daniel Hauke, Ph.D. student, is particularly noteworthy. Daniel has independently conducted a large clinical study (N=80) using multimodal neuroimaging (EEG and fMRI) in ultra-high risk and first-episode psychosis patients. This research has been recognized at international conferences, including Best Poster and Early Career Research awards at Schizophrenia International Research Society three years in a row, and by funding agencies, such as the Doc.Mobility Swiss National Science Foundation and Hejuba awards. Daniel graduated with Summa Cum Laude receiving the highest grade and recognition for his PhD thesis.

It is also important to highlight the work of Dr. Povilas Karvelis, a postdoctoral fellow, who has advanced novel computational models for suicide risk assessment, and who this year also received a CIHR postdoctoral fellowship, which will support his work bringing these computational models to the clinic.

Whole Person and Population Modelling Team

Team Lead: Dr. Daniel Felsky

The past year has been an important one for Whole Person and Population Modelling team. Progress has been made on several fronts, including the first publication officially developing the “Whole-Person” nomenclature in integrative mental health research, and several new initiatives in using the approach to improve the lives of elderly at risk for and suffering from dementia.

As part of the Toronto Dementia Research Alliance, Dr. Felsky secured two external grants as co-PI, totaling over $2.5 million. Funding will be used to develop machine learning and AI-based algorithms expedite triage of memory concerns in multiple Toronto clinics, in collaboration with Dr. Morris Freedman at Baycrest, and to learn how to predict different subtypes of neurodegeneration with novel blood-based biomarkers and neuroimaging in collaboration with Dr. Carmela Tartaglia at UHN. Work to integrate biopsychosocial data in other populations has also seen major steps forward, with Dr. Felsky’s group leading data analytics for the first Annual General Meeting of the TAY CAMH Cohort study, which has now recruited and assessed over 250 young participants.

The team has had many milestones to celebrate this past year. Dr. Felsky graduated three students in the summer of 2022, including an IMS PhD transfer (Earvin Tio), and two co-supervised MSc thesis defenses (Jonas Rybnicek and Amin Kharaghani). In addition, all four postdoctoral fellows on the team are now supported by competitive fellowships, including national and provincial awards. Finally, within just the last year, trainees on the team had 14 oral and poster presentations accepted at major international conferences, plus an additional four accepted at national and local events. Many of these have been or will be attended in person, which, for many trainees, represents their first opportunity to travel abroad for a scientific conference.

Finally, Dr. Felsky was nominated and voted in to join the Canadian Statistical Sciences Institute (CANSSI) Strategic Training for Advanced Genetic Epidemiology (STAGE) program as a Mentor, and was awarded a prestigious Investigator Travel Award from the American College of Neuropsychopharmacology.

Digital Health and Artificial Intelligence Team

Team Lead: Dr. Abhishek Pratap

The Digital Health and Artificial Intelligence team is focused on developing human-augmented solutions for mental health with real-world application. These research efforts will help improve long-term outcomes for people living with mental illness and move the world closer to personalized medicine in mental health care.

A significant focus of the team over the past year has been recruiting and onboarding a team of diverse experts in wearable tech for the Wearable Operations in Real-World Settings, or WearOPS, project. Wearable devices, such as smartwatches, rings, and vests, provide a wealth of continual physiological data such as heart rate, calories burnt, sleep patterns, temperature, and blood oxygen saturation. There is growing interest in leveraging wearables in decentralized trials to reach and recruit diverse target populations in a more efficient and less expensive manner than in traditional in-person trials. Wearable tech also enables the continual collection of real-world data through personalized sensing in naturalistic settings. Ongoing early research has demonstrated the enormous potential of wearable tech in mental health research and care.

The WearOps team aims to bring the crucial stakeholders—including manufacturers, researchers, privacy experts, clinicians to participants/patients, and their families—to develop an efficient and transparent system for enabling wearable research. The WearOPS overall process ranges from selecting and configuring fit-for-purpose devices to using machine learning and artificial intelligence methods to create robust and transparently validated digital biomarkers linked to clinical outcomes of interest in a target population.

Krembil Centre for Neuroinformatics leadership has initiated the recruitment process for an Independent Scientist in AI and Digital Health to succeed Dr. Abhishek Pratap. An international search will be conducted to identify leading candidates to further the mission and objectives of the Krembil Centre and CAMH to advance artificial intelligence and digital health innovation in service of patients locally and globally.

On-going related research

SleepHealth

The SleepHealth Mobile App Study aims to understand real-world factors impacting people's sleep and daytime functioning in naturalistic settings. Study participants completed surveys related to sleep health during onboarding along with sleep diaries documenting factors affecting their daily sleep.

Wash Study

A smartphone sensor data analytics project that deals with a full set of heterogeneous datasets to be correlated with mood analysis and mental health. The acquired data includes periodically-promoted user survey entries, light sensor output, Bluetooth and WiFi status, GPS data, and multivariate IMU time series.

Zephyr: Bipolar Disorder Patients' Postural Dynamics

A wearable sensor data analytics project that deals with bipolar disorder patients' posture and activity data collected using a chest-worn wearable. Patients' posture is processed, featurized, analyzed throughout 24 hours, and clustered.

Events & Knowledge Sharing

This year saw the Krembil Centre for Neuroinformatics, fueled by your support, 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. As we emerge from the COVID-19 pandemic, we look forward to hosting more face-to-face opportunities to build on the great progress our teams have made virtually.

Krembil² Event

The Krembil² Retreat was held on June 2 in Toronto and highlighted current and future collaboration opportunities between the Krembil Centre and the Krembil Brain Institute at University Health Network (UHN). Researchers came together, in person and virtually, to help advance the critical work of these two institutions by identifying new opportunities to expand collaboration and exploring strategies to build new bridges to accelerate discoveries that bridge mental health and brain disorders.

"Krembil² is our opportunity to celebrate the synergies between two great organizations and find further areas of convergence between our research and clinical services. Ultimately, our collaboration will allow us to better understand all levels of the brain, from genes to circuits, whole brains to the whole person to better define and treat mental illnesses. We hope to build Toronto's reputation as beacon of brain sciences and data."

Dr. Sean Hill, Director of the Krembil Centre for Neuroinformatics at CAMH

In the spirit of institutional collaboration, participants discussed the work that is well underway to leverage and expand the BrainHealth Databank. Researchers also reiterated that the brain is just one part of the equation and must not be viewed in isolation from the rest of the body. By adjusting data collection methods with this important fact in mind, researchers will hone in on the opportunity to collect and share more high-quality data.

The Krembil² Retreat facilitated connections across all levels of the organization, from researchers to trainees. During the retreat, trainees presented their research, offering a valuable opportunity to promote joint-institutional mentorship and education. Trainees also shared their perspectives about how to streamline processes, enhance training and improve tools to allow them to maximize their impact now and into the future.

On the heels of a very successful and productive event this year, both organizations are looking forward to hosting the next Krembil² Retreat in summer 2023.

In the five short years since the inauguration of the Krembil Centre for Neuroinformatics, it has become recognized as a global leader in neuroinformatics and is taking a unique approach to collaboration in this space. By bridging the two Centres, we will aim to provide a framework agreement and resources to support a broad array of collaborations including:

- Discover, facilitate and streamline scientific collaboration
- Support and enhance any existing collaborations
- Develop shared infrastructure for data management and analysis
- Simplify and standardize data sharing agreements for rapid collaboration
- Advance machine learning and computational methodologies
- Accelerate integrated educational programs and knowledge transfer
- Cross-supervision of trainees and co-development
- BrainHealth Databank—an inter-institutional resource for open science sharing of consented patient trajectory data

Krembil Centre for Neuroinformatics Summer School

Building on the success of previous KCNI Summer School sessions, and with the lessening of COVID-19 restrictions, organizers of this year's session were thrilled to host students in person. From July 4 to 9, 18 trainees participated in a new collaborative course being piloted that focused on "learning by doing." Learners were graduate students, medical students and postdoctoral fellows from the Krembil Centre, current local collaborators (UHN,) and future collaborating research groups throughout Ontario.

Institutions Represented:

CAMH

University of Toronto

Krembil Research Institute/UHN

Carlton University

University of Waterloo

McMaster University

Windsor University School of Medicine

Led by Krembil Centre scientists and a team of 10 teaching assistants, participants were introduced to the concepts and methods behind psychiatric neuroinformatics—encompassing genetics, brain structure and function, and cognition. This unique learning opportunity aims 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.

To help students prepare in advance of the week, organizers published the KCNI School Virtual Learning Series, a virtual learning series of over 40 hours of YouTube content—organized into playlists with accompanying links to materials (code, demo data and software). They accompanied the release of these materials with a series of publicly advertised question-and-answer sessions with Krembil Centre for Neuroinformatics.

Among many highlights from the week, were the "fireside-chat" discussions with invited CAMH researchers and clinicians and the opportunity to visit the labs of leading neuroscientists, including Dr. Taufik Valiante and Dr. Karun Singh at the Krembil Research Institute at UHN.

Social Media Discussion and Praise of KCNI Summer School

From KCNI School Instructors and TAs:

@DaveMomi

Pleasantly overwhelmed by day #1 of @CAMH_KCNI summer school. This is what science is all about lot of talented students and....food of course

@neuronJoy

Day 3 of our @CAMH_KCNI summer school involved a site-visit to @KBI_UHN to visit the labs of @DrValiante and @karunsinghneuro to check out some super cool tissue cultures and organoids and patch clamping. Single-cell analysis continues! #KrembilNeuroinformatics

@DanielFelsky

Learning about care pathways and clinical context in the treatment of #mentalillness with clinician-scientists @victormarktang and @JonesBdm for our @CAMH_KCNI summer academy. @CAMHResearch

@mabdelhack

Final day of the @CAMH_KCNI summer school and groups are presenting their hard work

Krembil Centre UHN Scientists:

@DrValiante

Love it!! Can see @MadeleineFalby in the thick of it on the computer and in the lab. @neuronJoy what a great idea for the visit!!

@karunsinghneuro

What a great course organized by @neuronJoy for trainees!

Hands-on project-based learning

Participants were mentored by Krembil Centre scientists as they completed intensive group projects matched to their interests over the course of the week. These projects were designed to enable participants to build mastery in selected integrative research methods. Students presented their group project to the group at the conclusion of Project Week.

Project 1:

In the integrative (genomics to microcircuits) project

Project Lead – Dr. Dan Felsky

Students learned how to analyze admixed individuals in the context of genome-wide association and then how to feed genomic results forward into microcircuit models.

Project 2:

Single Cell Transcriptomics

Project Lead – Dr. Shreejoy Tripathy

Students learned about integrative analysis of mouse and human single-cell gene expression data. What are conserved cell types in the brain and what are their characteristics?

Project 3:

fMRI based Whole Brain Modeling

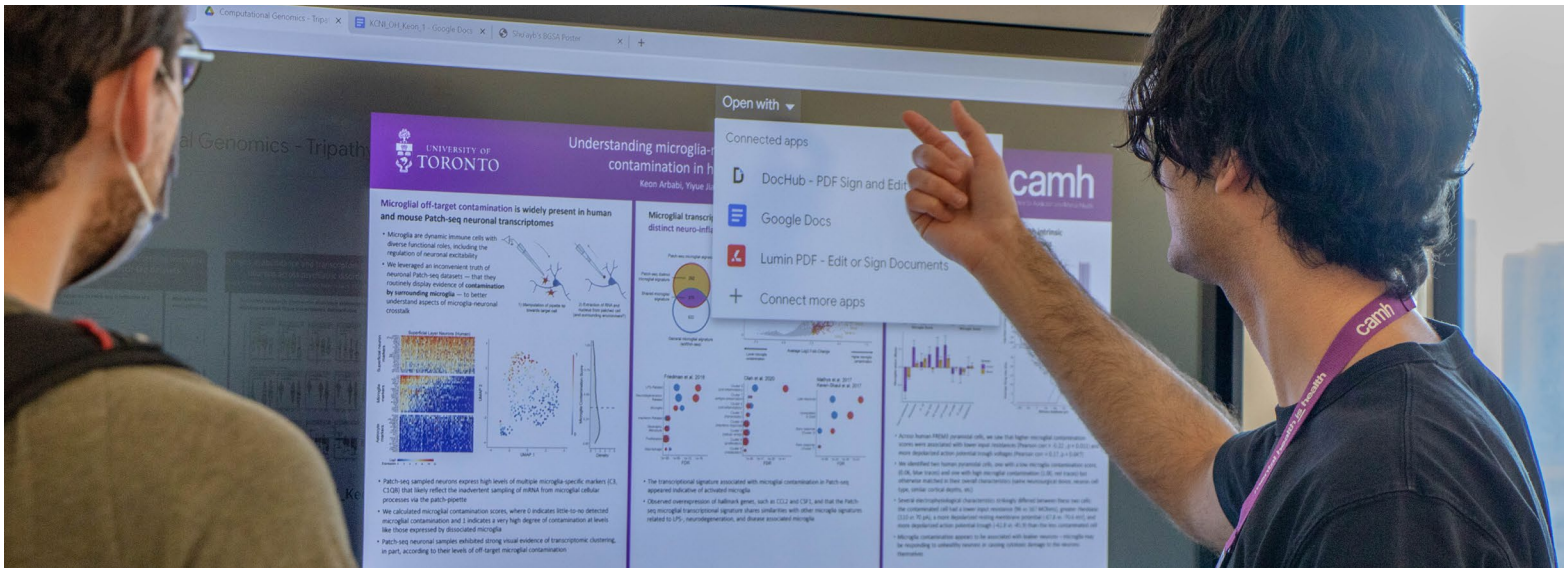
Project Lead – Dr. John Griffiths

Students learned how to use computational network models of neuroimaging data to identify physiological mechanisms and signatures of mental illness.

KCNI Open House

On June 24, the KCNI enthusiastically welcomed its community to visit the Krembil Centre and meet the team. The Centre hosted over 85 attendees in person and more than 60 attendees online throughout the day. The entire Krembil Centre team is proud of their continued progress and enjoyed showcasing the achievements, contributions and collaborative efforts of the past year. The day featured opening remarks by Dr. Sean Hill and Dr. Damian Jankowicz, updates from the Krembil Centre Lab Leads and spotlight and poster presentations from the Krembil Centre trainees.

Click here to watch recordings from the KCNI Open House.



Thank you

Thank you for your continued leadership support of the Krembil Centre for Neuroinformatics and CAMH. 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
List of Publications

KCNI Scientist Publications (Oct 1, 2021 to Sep 30, 2022)

Wainberg, M., Jacobs, G. R., Voineskos, A. N. & Tripathy, S. J. Neurobiological, familial and genetic risk factors for dimensional psychopathology in the Adolescent Brain Cognitive Development study. *Mol. Psychiatry* **27**, 2731–2741 (2022)

Kim, E. H., Howard, D., Chen, Y., Tripathy, S. J. & French, L. LaminaRGeneVis: A Tool to Visualize Gene Expression Across the Laminar Architecture of the Human Neocortex. *Front. Neuroinform.* **16**, 753770 (2022)

Gillespie, T. H., Tripathy, S. J., Sy, M. F., Martone, M. E. & Hill, S. L. The Neuron Phenotype Ontology: A FAIR Approach to Proposing and Classifying Neuronal Types. *Neuroinformatics* (2022) doi:10.1007/s12021-022-09566-7

Wainberg, M. et al. Deletion of Loss-of-Function–Intolerant Genes and Risk of 5 Psychiatric Disorders. *JAMA Psychiatry* **79**, 78–81 (2022)

Reduced inhibition in depression impairs stimulus processing. *https://www.cell.com › cell-reports › pdfhttps://www.cell.com › cell-reports › pdf*

Guet-McCreight, A. *et al*. Age-dependent increased sag current in human pyramidal neurons dampens baseline cortical activity. *bioRxiv* 2021.11.03.467014 (2022) doi:10.1101/2021.11.03.467014

Gutman, B. A. et al. A meta-analysis of deep brain structural shape and asymmetry abnormalities in 2,833 individuals with schizophrenia compared with 3,929 healthy volunteers via the ENIGMA Consortium. *Hum. Brain Mapp.* **43**, 352–372 (2022)

Human peripheral monocytes capture elements of the state of. *https://europepmc.org › article › ppr › ppr442832https://europepmc.org › article › ppr › ppr442832*

Gao, Y. *et al.* Integration of GWAS and brain transcriptomic analyses in a multiethnic sample of 35,245 older adults identifies DCDC2 gene as predictor of episodic memory maintenance. *Alzheimers. Dement.* (2021) doi:10.1002/alz.12524

Roostaei, T. *et al.* Proximal and distal effects of genetic susceptibility to multiple sclerosis on the T cell epigenome. *Nat. Commun.* **12**, 1–12 (2021)

Ma, Y. *et al*. Atlas of RNA editing events affecting protein expression in aged and Alzheimer's disease human brain tissue. *Nat. Commun.* **12**, 1–16 (2021)

Hueniken, K. *et al*. Machine Learning–Based Predictive Modeling of Anxiety and Depressive Symptoms During 8 Months of the COVID-19 Global Pandemic: Repeated Cross-sectional Survey Study. *JMIR Mental Health* **8**, e32876 (2021)

Wainberg, M. *et al.* Association of accelerometer-derived sleep measures with lifetime psychiatric diagnoses: A cross-sectional study of 89,205 participants from the UK Biobank. *PLoS Med.* **18**, e1003782 (2021)

Karvelis, P. *et al*. Computational approaches to treatment response prediction in major depression using brain activity and behavioral data: A systematic review. *Network Neuroscience* 1–38 doi:10.1162/netn_a_00233

Karvelis, P. & Diaconescu, A. O. A Computational Model of Hopelessness and Active-Escape Bias in Suicidality. *Computational Psychiatry* **6**, 34–59 (2022)

Hauke, D. J. *et al.* Increased Belief Instability in Psychotic Disorders Predicts Treatment Response to Metacognitive Training. *Schizophr. Bull*. **48**, 826–838 (2022)

Renn, B. N., Schurr, M., Zaslavsky, O. & Pratap, A. Artificial Intelligence: An Interprofessional Perspective on Implications for Geriatric Mental Health Research and Care. *Front. Psychiatry* **12**, 734909 (2021)

Olaye, I. M. *et al*. Recommendations for Defining and Reporting Adherence Measured by Biometric Monitoring Technologies: Systematic Review. *J. Med. Internet Res*. **24**, e33537 (2022)

Goodday, S. M. *et al*. An Alternative to the Light Touch Digital Health Remote Study: The Stress and Recovery in Frontline COVID-19 Health Care Workers Study. *JMIR Form Res* **5**, e32165 (2021)

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Maslej, M. M., Shen, N., Kassam, I., Rodak, T. & Sikstrom, L. Race and Racialization in Mental Health Research and Implications for Developing and Evaluating Machine Learning Models: A Rapid Review. *Stud. Health Technol. Inform*. **290**, 1088–1089 (2022)

Griffiths, J. D., Bastiaens, S. P. & Kaboodvand, N. Whole-Brain Modelling: Past, Present, and Future. *Adv. Exp. Med. Biol*. **1359**, 313–355 (2022)

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Northoff, G. et al. Augmenting Human Selves Through Artificial Agents - Lessons From the Brain. *Front. Comput. Neurosci.* **16**, 892354 (2022)

Mazza, F., Valiante, T. A., Griffiths, J. D. & Hay, E. EEG biomarkers of reduced inhibition in human cortical microcircuits in depression. *bioRxiv* 2021.07.18.452836 (2021) doi:10.1101/2021.07.18.452836

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Iavarone, E. *et al*. Reconstruction and simulation of thalamoreticular microcircuitry. *bioRxiv* 2022.02.28.482273 (2022) doi:10.1101/2022.02.28.482273

Sikstrom, L. *et al*. Conceptualising fairness: three pillars for medical algorithms and health equity. *BMJ Health Care Inform* **29**, (2022)

Mirjalili, M., Zomorrodi, R., Daskalakis, Z. J., Hill, S. & Rajji, T. K. Individualized real-time prediction of working memory performance by classifying electroencephalography signals. *Int. J. Imaging Syst. Technol.* **32**, 575–589 (2022)

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