

STRATEGIC PLAN 2021-2025

Douglas
CENTRE DE RECHERCHE
RESEARCH CENTRE

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The Douglas Research Centre in Context

A long history of excellence



Figure 1. The Douglas Institute

The Douglas Research Centre (DRC) enjoys a rich history that is intertwined with that of the Douglas Hospital (founded in 1881). Its academic mission dates back to 1930, when mental health research was first carried out at the Douglas, and well before the official creation of the Research Centre in 1979. From the pioneering work of Lehmann who introduced modern pharmacological treatments in North America to more recent work, the DRC has established itself as a leader in mental health research and continues to pursue innovation and excellence.

The Douglas: a world leader

The DRC is located in an integrated mental healthcare environment, the Douglas Mental Health University Institute, itself a facility in the Montreal West Island (MWI) Integrated University Health and Social Services Centre (CIUSSS). An important aspect of research activities is improving clinical care in mental health in a wide variety of specialized and ultra-specialized services that target populations of all ages. Research at the Douglas is internationally renowned, and the DRC is regularly ranked among the top 40 best teaching hospitals in Canada. Together, its 60 researchers hold 8 Canada Research Chairs, 1 FRQS Research Chair, and 3 other endowed or private chairs (Table 1). Additionally, the DRC trains nearly 250 students annually and receives 24 salary awards (researchers and students). The DRC is awarded an average of 27M\$ in grant funds every year, and its researchers collectively produce over 450 publications every year.

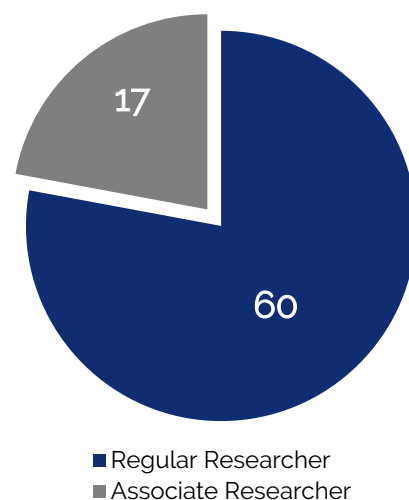


Figure 2. Distribution of researchers at the DRC

Table 1. Chairs and Titles of Distinction Held at the DRC

Canada Research Chair		FRQS Research Chair	
Tier 1		Lepage	Cognitive Neuroscience and Schizophrenia
Giros	Neurobiology of Mental Disorders	Endowed Chairs and Private Fellows	
Kieffer	Neurobiology of Addictions and Mood Disorders	Breitner	Pfizer Chair in Dementia Research
Malla	Early Psychosis	Serge Gauthier	Chair in Aging Studies
Turecki	Major Depressive Disorder and Suicide	In the process of attribution	Marguerite Bourgeois Research Chair
Tier 2		Titles of Distinction	
Brandon	Neural Circuits of Memory	Martin Lepage	James McGill Professor
Ernst	Psychiatric Genetics	Michael Meaney	James McGill Professor
Geoffroy	Youth Suicide Prevention	Natasha Rajah	CIHR Sex and Gender Science Chair
Villeneuve	Early Detection of Alzheimer's Disease		

Our Aspirations

Mission

UNDERSTAND, PREVENT, AND TREAT MENTAL DISORDERS THROUGH SCIENCE.

Vision

CREATE INNOVATIVE AND INTEGRATED RESEARCH PROGRAMS IN MENTAL DISORDERS, FROM GENES TO SOCIETY.

Values

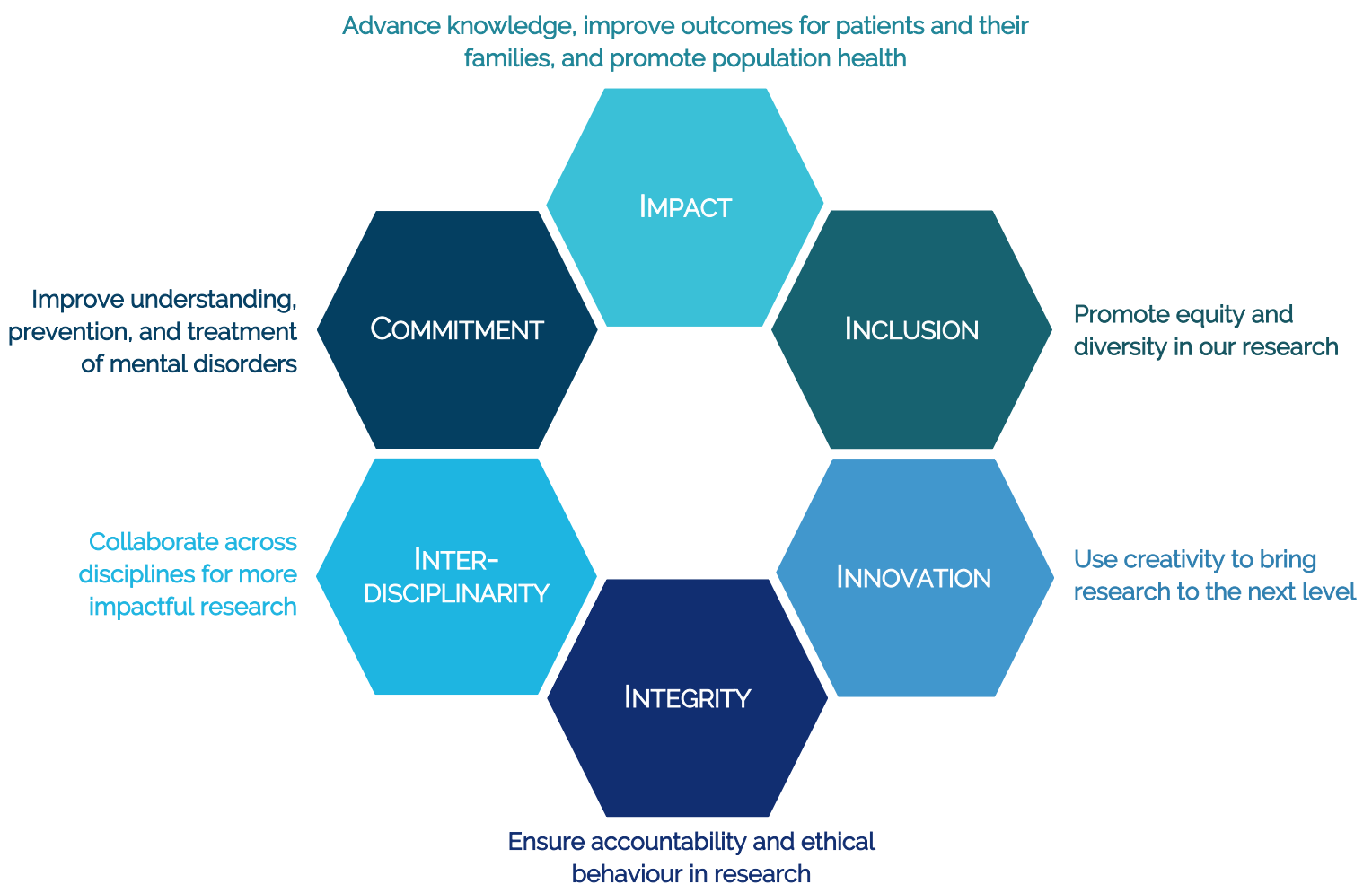


Figure 3. DRC Values

Goals

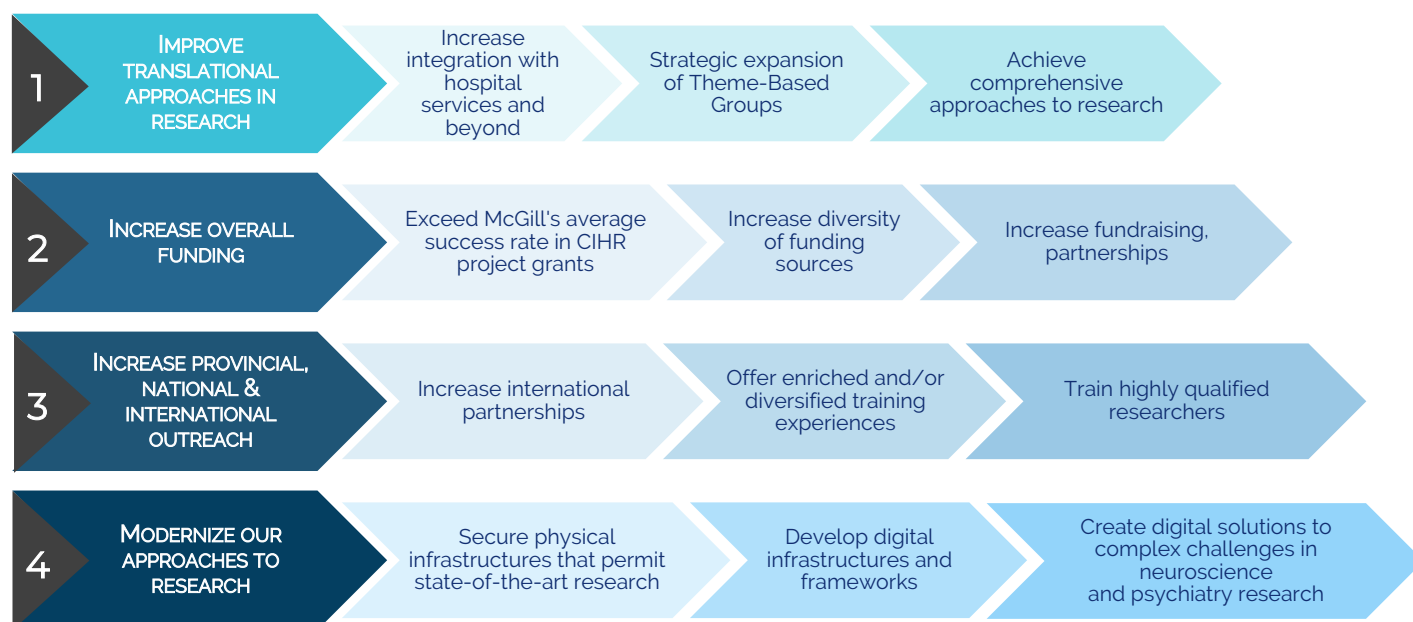


Figure 4. Strategic Goals for the DRC 2021-2025

Why now?

In 2018, the leadership of the DRC changed and a unifying desire among the researchers was to reaffirm the Douglas as a centre for excellence in mental health research. Through an initial consultation process, which included a well-attended in-person retreat in 2019, a number of steps were outlined to ensure both a scientific and organizational restructuring of the DRC that would meet everyone's needs. Restructuring was carried out over a period of 12 months during which time procedures were designed and implemented in collaboration with the researchers. The restructuring of the DRC activities was carried out with a desire to contribute to the overarching strategic plan of the research centre and is based on the belief that a unified vision and an organization that includes everyone's perspectives and needs will lead to a more efficient and more productive research environment.

Meeting Our Objectives

Defining a roadmap

1. Restructuring the DRC to better reflect the needs and orientations of the researchers

Development of a multi-layered structure that accounts for the type of research (discipline), the subject of the research (themes), and support structures to enable research to be successfully carried out (infrastructure support, i.e. platforms; regulatory support, i.e. standing committees and services to researchers).

1.1 Creation of research divisions

Research divisions are an essential mechanism to ensure that: 1) Every researcher of the DRC has a group in which they belong, 2) Material needs related to research approaches can be governed and shared by a unifying structure. The four research divisions were selected by consensus by the researchers as a whole, who self-identified with one of each division.

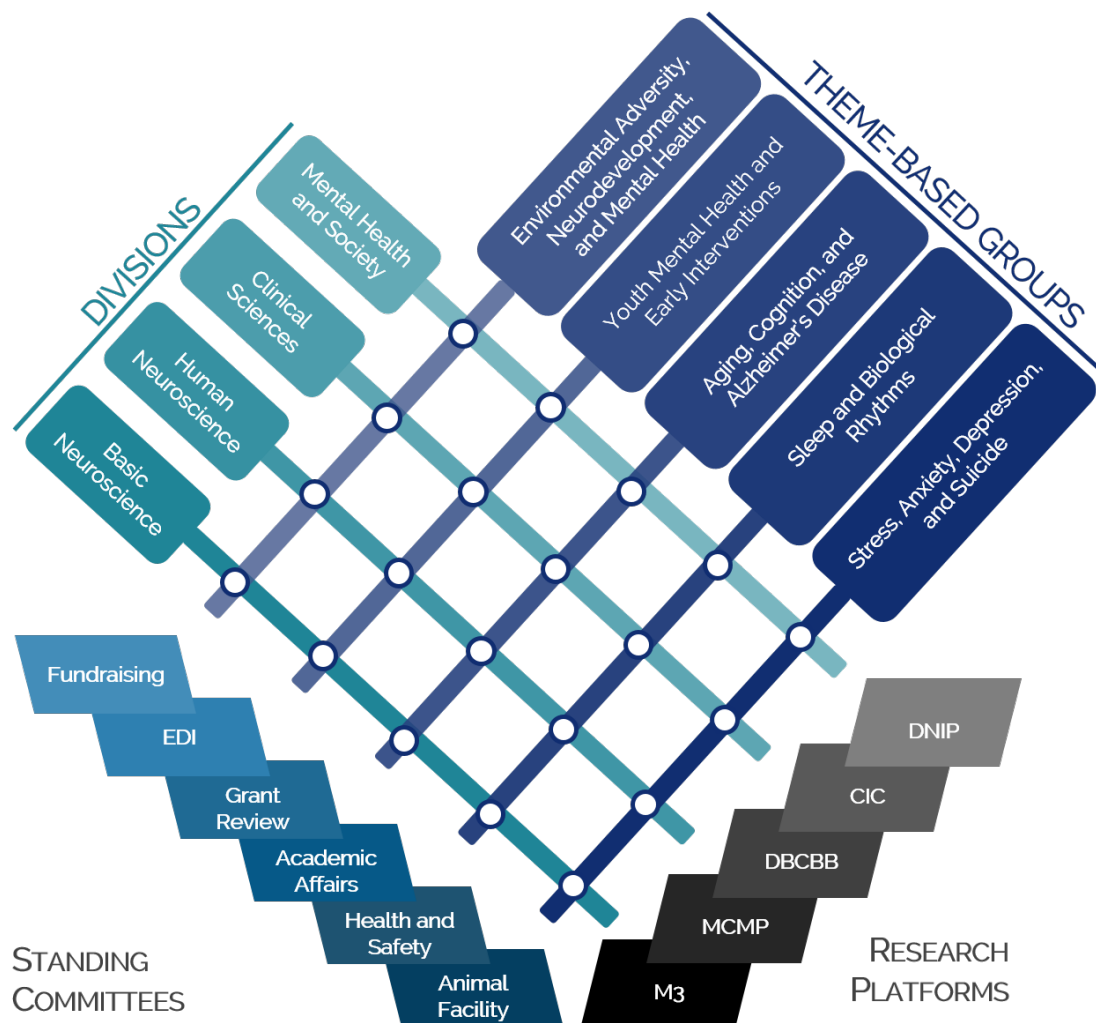


Figure 5. Structure of the DRC

Mental Health and Society – Leader: Xiangfei Meng, PhD

The Mental Health and Society division has the mandate to contribute to advancing psychological and social knowledge in mental health. Its objectives are, among others, to increase research on the organization of mental health and addictions services, social, cultural, and economic factors that contribute to mental health or addiction issues in the population to promote the development of better policies, directions, and services in mental health.

Clinical Research – Leader: Romina Mizrahi, MD, PhD

The Clinical Research division focuses on studying mental disorders through a variety of angles, including disease etiology, diagnosis, treatment, and prevention. Clinical research activities involve human participants, often in conjunction with laboratory data. This area of research activity is supported by the Centre for Advancement of Clinical Research.

Human Neuroscience – Leader: Sylvia Villeneuve, PhD

Capitalizing on its unique expertise, the Human Neuroscience division uses access to cellular models, human tissues, and human subjects to study the neurobiological mechanisms involved in a wide array of mental disorders, ranging from schizophrenia to dementia, and including sleep disorders, depression, and addictions. This division makes use of the [Cerebral Imaging Centre](#), a unique infrastructure that allows for the imaging of both human and animal brains, as well as the [Douglas-Bell Canada Brain Bank](#), which is a rare and unique international resource.

Basic Neuroscience – Leader: Sylvain Williams, PhD

The Basic Neuroscience division utilizes innovative techniques and exceptional expertise in model animals of psychiatric disease to improve our understanding of neurobiological mechanisms associated with physiological and behavioural changes that occur in mental disorders. The mission of the Basic Neuroscience researchers at the DRC is to contribute to making the Douglas the first international institute for translational neurobehavioural research in psychiatry in Canada. Our goal is to apply our substantial expertise in basic neuroscience investigation using animal modelling towards achieving a translational approach to research on mental disorders. This approach is critical and will depend on cross-divisional communication, collaborations and interactions with the theme-based groups (below).

The work of this division is supported through the Animal Facility, which possesses all the required tools for the analysis and characterization of animal behaviour, the [McGill-Mouse-Miniscope \(M3\) Platform](#), which uses state-of-the-art techniques to study brain functions associated with behaviour, and through the [Molecular and Cellular Microscopy Platform](#), which uses advanced microscopy techniques for basic and human neuroscience research.

1.2 Theme-based groups

Beyond the various methodological approaches used in neuroscience and psychiatry research, the mission of the Douglas can be best understood through the research themes that combine these different approaches to bring important research questions into focus. Theme-based groups (TBGs) were created as a mechanism to promote multidisciplinary research focused on specific areas, thus creating opportunities for collaboration and innovation. TBGs were competitively selected by external peer review and represent domains in which the Douglas has both clear leadership and opportunities for further development. As such, they embody the DRC strategic research priorities and include domains where growth through future recruitment will take place. Ultimately, reframing research questions within multidisciplinary TBGs has the potential to provide more complete, more competitive, and more successful research teams.

Theme-based groups were identified through a multi-stage process culminating in a final selection by an external committee (created and managed by the VPRIR of McGill Faculty of Medicine). The five TBGs created are:

- Environmental Adversity, Neurodevelopment, and Mental Health – Leader: **Patrícia Pelufo Silveira, MD, PhD**
- Youth Mental Health and Early Intervention – Leader: **Ridha Joober, MD, PhD**
- Stress, Anxiety, Depression, and Suicide – Leader: **Naguib Mechawar, PhD**
- Sleep and Biological Rhythms – Leader: **Nicolas Cermakian, PhD**
- Aging, Cognition and Alzheimer’s Disease – Leader: **Pedro Rosa-Neto, MD, PhD**

The TBGs are further detailed in the [Strategic orientations](#) section below.

1.3 Research Platforms

Douglas-Bell Canada Brain Bank (DBCBB) – Director: Naguib Mechawar, PhD

The DBCBB is the largest brain bank in Canada. It coordinates the brain donation process, prepares and stores the brain specimens and distributes samples to qualified researchers throughout the world in order to advance fundamental research

on mental disorders using valuable and donated human tissues. Tissue samples from donated brains give direct access to the cells, proteins and genes potentially implicated in the disease.

Its mission is to provide the scientific community with brain samples preserved under optimal conditions for research that will lead to advances in the treatment, cure and prevention of brain disease and disorders.

Molecular and Cellular Microscopy Platform (MCMP) – Director: Naguib Mechawar, PhD

The MCMP is an advanced optical microscopy core facility founded in 2015 that offers access to the latest fluorescence microscopy techniques for neuroscience research. The facility is an Olympus Discovery Centre, born from a partnership between the DRC and Olympus Canada Inc. This allows the MCMP to offer the latest microscopes and techniques at competitive rates compared with other core facilities. The Molecular and Cellular Microscopy Platform offers one-on-one support and training for fluorescence microscopy experiments and image analysis. The facility is qualified in a range of imaging tasks from basic neuron reconstruction to high-speed, deep-tissue optogenetic experiments in brain slices or live animals.

Its mission is to help students and researchers alike to plan, design, perform, and analyze fluorescence microscopy experiments.

Cerebral Imaging Centre (CIC) – Director: Mallar Chakravarty, PhD

The CIC is a new state-of-the-art facility dedicated to conducting preclinical and clinical brain imaging research in the field of mental health. It was conceived as an incubator for translational research, where animal imaging studies would serve to enrich the knowledge base derived from human studies and vice versa.

Its mission is to foster the development of novel biomarkers for early diagnosis, treatment and prevention of neuropsychiatric conditions.

McGill-Mouse-Miniscop Platform (M3) – Directors: Sylvain Williams, PhD & Mark Brandon, PhD

The M3 Touchscreen Behaviour Platform is a cohesive imaging and behavioural neuroscience research laboratory. The platform is continually developing and testing novel approaches for understanding and decoding brain and circuit function and we are eager to share our capabilities with the greater neuroscience community.

Its mission is to develop new expertise and technologies that bridge the research findings between mouse and human.

Douglas Neuroinformatics Platform (DNIP) – Director: Mallar Chakravarty, PhD

The DNIP is a new core facility aimed at supporting longitudinal monitoring and prediction of clinical trajectories. The platform focuses on developing an iterative and engaging implementation plan to support the proposed interventions, uptake, and ethical use of new technology in mental healthcare (respecting patient's rights, privacy, safety and efficient use of resources). These are unique challenges that require a unique combination of local leadership and innovation in terms of data capture and integration with the local members of the CIUSSS. Future goals for this centre include the development of large-scale collaborative endeavours with other major research, start-up incubators within the Douglas Research Centre, fee-for-service services that integrate with other digital mental health/psychiatry initiatives, and for testing and formal trials of new technologies, and expertise that will allow for examining clinical trial data.

Its mission is to improve care with the latest in digital technologies that can be used for assessment and to use machine learning and informatics to move closer to precision medicine in psychiatry.

1.4 Standing committees

Standing Committees have been established to address the needs identified by Douglas researchers during consultation sessions. The established committees are:

- Douglas Facility Animal Care Committee – Chair: **Tak Pan Wong, PhD**
- Douglas Health & Safety Committee – Chair: **Lalit Srivastava, PhD**
- Fundraising Committee – Chair: **Carl Ernst, PhD**
- Academic Affairs Committee – Chair: **Nicolas Cermakian, PhD**
- Equity, Diversity, and Inclusion Committee – Chair: **Natasha Rajah, PhD**
- Grant Review Committee – Chair: **Patricia Boksa, PhD**

Each of the standing committees is governed by a Chair and has an obligation to adhere to their written mandate (provided by the executive committee) as well as to keep written records of each meeting. Standing committees are reviewed once per year to ensure that their work is relevant and responds to an existing need.

1.5 Research support services

In addition to these DRC structures, other mechanisms for ensuring adequate support for researchers have been developed in collaboration with our key partners. Among them are mechanisms for ensuring ethical conduct in research (FRQS Research integrity officer, **J.B. Debrulle**; the Research Ethics Board, chaired by **J. Rochford**, working in collaboration with the MWI-CIUSSS) and a research support office, developed as a collaborative entity, co-managed by the DRC and the Directorate for Academic, University, Educational, and Research Affairs (DAUER), MWI-CIUSSS, to adapt to the ever-evolving needs of research.

Collectively, the goal of these support services is to work with researchers to improve, facilitate, and promote ground-breaking research in mental health.

2. Establishing a clear model of governance

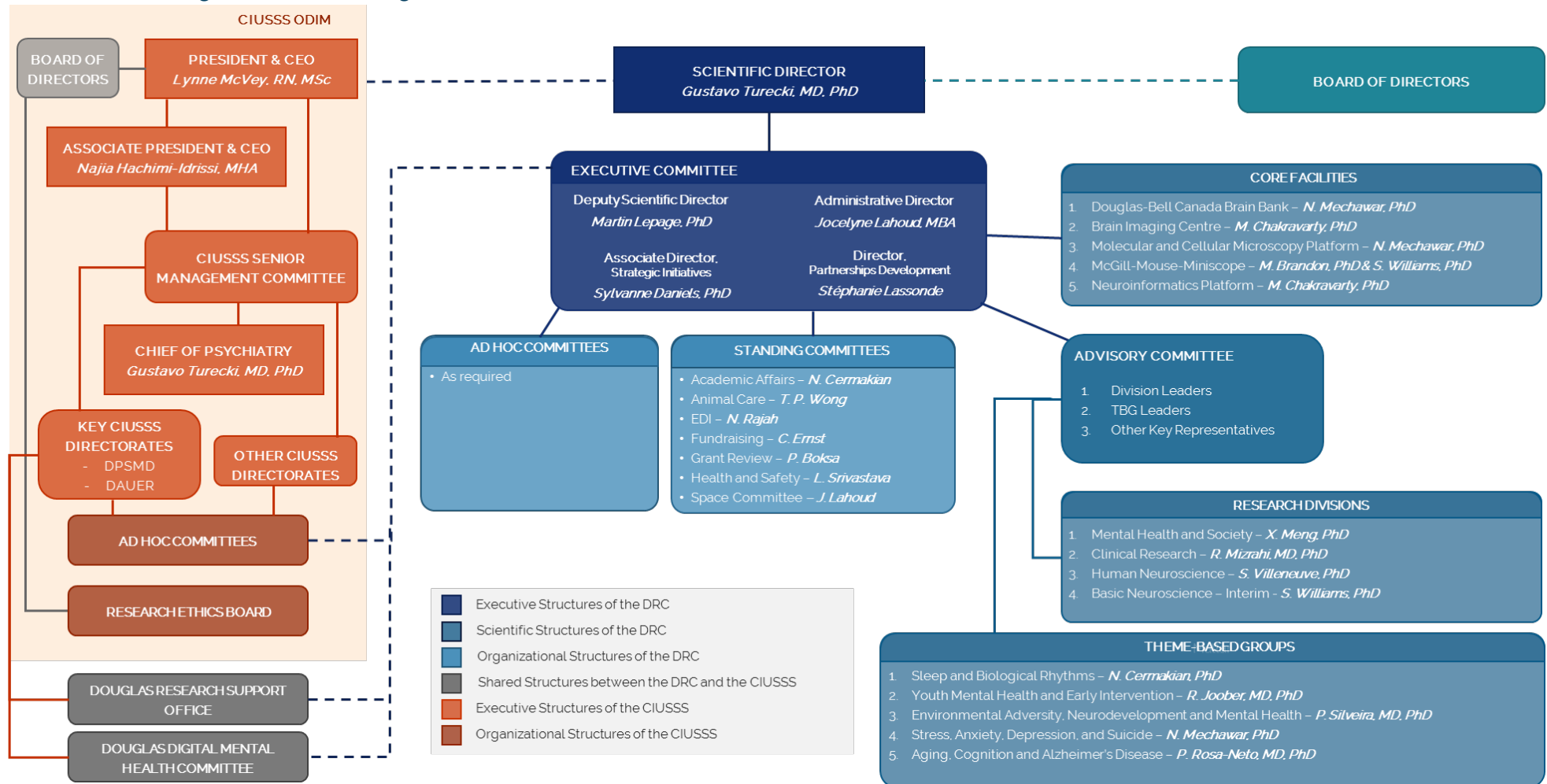


Figure 6. DRC Governance Model

3. Strengthening our infrastructures

Shared infrastructures are a key facet of our activities at the DRC, and infrastructure constraints have limited our growth over the last few years. One key direction for the Douglas is to invest in renewing our infrastructures. In January 2020, the Quebec government announced the approval of a major infrastructure project for the Douglas Institute, which promises to address some of the long-standing issues with the aging buildings at the Douglas Institute. We are actively contributing to the planning stages to ensure that this new infrastructure project will be aligned with our needs and goals moving forward. In addition to this major infrastructure development, the DRC will pursue opportunities to secure targeted equipment and infrastructure deemed essential for the development of the centre and that are complementary to the new hospital infrastructure. These opportunities will be developed in line with our strategic goals and orientations, as well as in partnership with key stakeholders, such as McGill and the Montreal West Island CIUSSS, to ensure that the DRC remains competitive and that innovation is fostered through state-of-the-art facilities.

We have identified potential areas for infrastructure investments.

3.1 Non-human primate platform

Typically, behavioural neuroscience investigations based on rodent models are limited by anatomical and physiological cross-species differences and complications related to translating therapeutic interventions to humans. The recent major investments at McGill University to curate Marmoset colonies and to establish one of the first transgenic Marmoset facilities in North America, has presented the Douglas with the opportunity to develop a non-human primate program and lead the next generation of psychiatric research using this animal model that presents clear advantages compared to rodents. Marmoset research has great promise to accelerate translational psychiatry and capitalizes on our existing expertise. This type of research is lacking in Canada and globally. The DRC already possesses expertise in using mental health-relevant behavioural approaches including work on marmoset with McGill-based PIs. This places us in an ideal position to be a leader in adapting such approaches from rodents to non-human primates, and as a consequence, will add an entirely new dimension to our research efforts in the basic neuroscience division. In particular, the fact that marmosets are social animals, with a higher order of communication than rodents, will increase the translational capabilities tremendously. The impact of this program will be further enhanced when combined with the imaging program described below. In order to accommodate this new program, in addition to increasing our capacity for rodent work, investments need to be made to expand on the existing animal facility space by building a dedicated area for marmoset research, to house modern touch-screen sensitive technology, robotic-assisted surgical instruments, as well as wireless electrophysiological and miniaturized microscopy recordings.

3.2 Translational imaging centre

The Douglas has state-of-the-art animal MRI facilities and expertise – already surpassing our competitors. This expertise is complemented by extensive methodological experience in behavioural phenotyping, in vivo physiology, cellular imaging, and epigenetics. We envision the creation of a true pipeline from non-invasive MRI imaging to detailed understanding of pathology in psychiatric models at the physiological, cellular, and epigenetic levels.

MRI and PET scanning

At the level of live animal imaging and in addition to MRI, the Douglas possesses extensive expertise and leadership in PET imaging and a very active research program using this approach. However, our investigators currently rely on offsite imaging infrastructure, to develop this aspect of our research. There is therefore a clear need to invest in this area both in infrastructure (PET scanner for human and pre-clinical imaging) and targeted

recruitment to greatly enhance the bandwidth of the Douglas's pipeline in translational imaging in psychiatric research. The creation of this translational pipeline from rodents to primates to humans will be unique internationally, and will allow structural, molecular and functional imaging to uncover biomarkers and explore molecular mechanisms of disease non-invasively.

Microscopy imaging

At the tissue level, new technologies for brain tissue clearing and light-sheet microscopy now allow for full-brain cellular imaging at a very rapid speed compared to older approaches. We already have the basic infrastructure on which we should build to include innovative new techniques such as expansion microscopy, which allows for nanoscale imaging of preserved brain specimens using conventional light microscopy by physically magnifying the specimen. This approach is ideal for imaging of complete brain circuits and for analyzing post-mortem brains, further enhancing the translational aspect of this program. For example, this would enable the visualization of synaptic contacts onto dendrites and spines, or neuronal-glial interactions, in healthy and pathologic brains of rodents, non-human primates, and humans.

3.4 Computational neuroscience and bioinformatics

As datasets become larger, multimodal, and more complex, new significant investments are needed in terms of data infrastructure. Expanding data infrastructure will transform the research capacity at the DRC by enabling fast access to local data servers and access to local compute nodes (both CPU and GPU) to develop analysis prior to using cloud services (i.e., Compute Canada).

4. Investing in our human resources

An important area for investment of time and resources is the expansion and renewal of our research workforce. We face an aging faculty, with a significant proportion of our researchers who are likely to retire within the next ten years. Additionally, we have actively developed certain key areas of research that would benefit from strategic hiring practices. Future hiring will be prioritized based on theme-based groups and the need for complementary expertise in new recruits. We are actively working with the CIUSSS, with McGill, and with the Douglas Foundation to secure the necessary support to proceed with much-needed recruitments.

Additional areas identified for increased time and financial investment include the creation of a peer-mentorship program for early-career investigators hired at the Douglas and the development of an enhanced training environment (through increased peer-based exchanges, including faculty meetings and standing seminar series, as well as by offering complementary training platforms such as the Knowledge transfer and implementation science (KTIS) training program currently in development).

Guiding principles

In line with our stated mission, we seek to understand, prevent, and treat mental disorders through science, using innovation and creativity. We are at a turning point in the history of the Douglas: several changes in the context in which we are operating have come together and provide us with an opportunity to reinvent our approaches, while staying true to our history and our values. At a time of changing technologies, it is imperative that we integrate digital approaches in the study, early detection, treatment, and follow-up of mental disorders. We also believe that we have a duty, not only to the scientific community, but to our funders and to the general public, to openly share our findings, our techniques, and our resources by adopting Open Science approaches, and that we invest in strategically-coherent, proactive knowledge transfer

initiatives. Through these combined approaches, we are confident that we can set a course for the Douglas that will ensure that it thrives as a place of scientific and clinical excellence.

1. Digital approaches to mental health

The Douglas has established itself as a leader in the treatment of mental disorders through innovative patient care. One area where the Douglas is committed to making significant investments is in digital technologies, in an initiative spearheaded by **Drs. Martin Lepage and Mallar Chakravarty**, with support from the CIUSSS DAUER (Geneviève Morin). In particular, there has been momentum in terms of **measurement-based care (MBC)**, data management, and digital approaches to services in mental health. MBC has the potential to provide timely, continuous, and quantitative estimations of treatment progress and define indices of quality of care, at both the individual and organizational levels. Ultimately, MBC results in improved patient outcomes and efficient use of resources. We are now ready to leverage the expertise we have already developed to make the Douglas a model of mental health care where technology is fully integrated in daily clinical decisions.

Drawing on our state-of-the-art capabilities in neuroinformatics and the rich resources at the Douglas, and considering the changing landscape of mental healthcare, we are well-situated to become leaders in digital health in Quebec, in Canada, and internationally. Our MBC approach, enabled by technology, will significantly increase our standards of care, whereas the development of digital mental health interventions will promote better access to innovative treatments. In the long-term, we are aiming for a full integration with clinical programs at the Douglas and the development of multi-centre initiatives that would be based on our technological developments. Our ambitions are fully aligned with the principles of the *Programme Québécois pour les troubles mentaux (PQPTM)*, which identifies MBC as one of its three pillars. **Ultimately, our goal is to become the national leader in digital mental health and MBC in mental health.**

Action plan: achieving our goals in the next 5 years

This will require an implementation plan to support the proposed interventions, uptake, and ethical use of new technology in mental healthcare (patient's rights, privacy, safety and efficient use of resources).

We have already secured the support of key leaders within our institution for our vision of enhanced digital mental health and will ensure that our initiative aligns well with the current development of the '*dossier santé numérique*' currently being developed by the MSSS.

Concrete steps required to bring this ambition to fruition include:

- Creating a Digital Mental Health Committee for the DRC
- Develop a robust CIUSSS/Douglas-wide digital transformation strategy
- Identifying key projects to champion our expertise in digital mental health
- Creating a framework for industry partnerships
- Developing productive partnerships with the digital industry and significant investment in our software/hardware/big data solutions
- Develop data acquisition harmonization SOPs to allow clinical, behaviour, biospecimen, and biomarker data integration using the upcoming DRC computational infrastructure.
- Contribute to the creation of a clinical data lake at the CIUSSS. Such a structure would create synergies and develop capacities for data-driven approaches, including AI approaches.

2. Open science approaches

Over the last few years, transparency has become one of the key features of science research. As a leading national institution in neuroscience and psychiatry research, it is our duty, not only toward the scientific community, but also toward funding agencies, decision-makers, and the general public, to share our results, our techniques, and our resources by adopting Open Science. Open Science is a broad concept that can be applied in many ways – and as such tailored to our needs. For example, at the Neuro, Open Science principles are defined as:

- *Share scientific data and resources*
- *Open external research partnerships*
- *Share research participants' contributions and protect their rights*
- *Do not file patents*
- *Respect academic autonomy.*¹

It is therefore incumbent upon us to thoroughly assess the unique needs, challenges, and benefits of implementing Open Science at the DRC, and to tailor an Open Science approach to the cultural, clinical, and research realities of our environment to ensure that we adopt a model that protects sensitive data while allowing us to share knowledge with others. Adopting Open Science is a necessity to ensure not only that we comply with existing requirements from funding agencies, but also as a key strategy to maximize our impact in our field, to promote forward-thinking, collaborative endeavours, and to maintain our legacy of excellence and innovation in mental health research and care.

Action plan: achieving our goals in the next 5 years

There is a clear appetite for Open Science at the Douglas, and we would like to build on the individual initiatives of certain platforms and early adopters to create a unified, institute-wide vision and policy around Open Science, all the while respecting the specific needs of individual researchers. Two of our core facilities (Douglas-Bell Canada Brain Bank, Cerebral Imaging Centre) and one of our major research initiatives (StoP-AD) have already taken steps to adopt Open Science methodologies and are pioneering this change at the Douglas. Our other core facilities and major research initiatives constitute ideal candidates for our next forays into adopting Open Science approaches.

To respect the unique research environment of the Douglas, these next steps will be taken after a consultative process over the course of 12-months, for which funding has already been secured through the Tannenbaum Open Science Institute. Our goal is to transform the Douglas into a leading Open Science institution in Canada.

Concrete steps to reach this goal include:

- Conduct a needs assessment with key stakeholders
- Develop a roadmap for implementing Open Science strategies at the DRC
- Create a framework to orient sustainable support and dissemination of Open Science at the DRC

¹ Poupon V, Seyller A, Rouleau GA. The Tanenbaum Open Science Institute: Leading a Paradigm Shift at the Montreal Neurological Institute. *Neuron* 2017;95(5):1002-1006. <https://www.sciencedirect.com/science/article/pii/S0896627317306487>

3. Knowledge transfer and implementation science

Knowledge transfer and implementation science (KTIS) are essential components of research activities. KTIS represents a continuum of activities from the publication of research results to developing collaborative practices, all of which aim to share knowledge and promote their use in practice, in decision-making contexts, or by the general public.² As KTIS components of research projects become more widely adopted and more diversified, we seek to develop proactive policies to encourage and support KTIS activities within our research community (described in detail in the *Politique en transfert de connaissances du CR Douglas*). Such policies depend on identifying key actors in KTIS processes in our research centre, including knowledge producers, knowledge users, and facilitators of KTIS (Figure 3). Key to the planning of KTIS activities are the pillars of our research approaches: developing translational research, espousing Open Science approaches, and involving knowledge users.

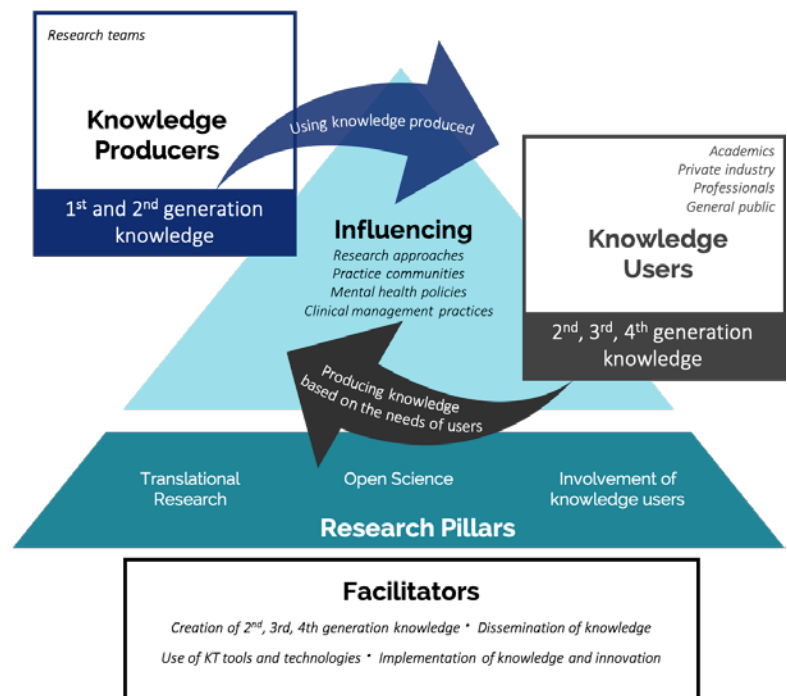


Figure 7. KTIS at the DRC

Action plan: achieving our goals in the next 5 years

Develop our KTIS in partnership with the DAUER, focusing on:

- Creating content adapted to different levels of users (scientific community, government or policy makers, service users, general public)
- Disseminating knowledge
- Implementing knowledge or innovation locally and experimentally

Concrete steps to reach our objective of enhancing KT activities at the DRC are:

- Giving researchers access to KT specialists for questions or support relating to their projects
- Increasing exposure of research to a broader audience (e.g. through the production and dissemination of videos based on research seminars, through social media campaigns and communication strategies)
- Creating a KT program and studio to help train students and staff to produce KT items related to their research activities

² Lemire, N., Souffez, K. et Laurendeau, M.-C., Animer un processus de transfert des connaissances: bilan des connaissances et outil d'animation. INSPQ (2009). 69 pages.

Strategic orientations

1. Environmental adversity, neurodevelopment, and mental health (Patrícia Pelufo Silveira, MD, PhD)

1.1 Need

Prenatal and early neonatal environments are important contributors to the subsequent risk for all common mental disorders. Most mental disorders show a peak age of onset in childhood or early adolescence, yet human epidemiological research generally focuses on genetic or environmental correlates of disease states using studies of adult subjects. The relative absence of epidemiological data prior to adulthood results in a major gap in our knowledge about the origins of psychopathology. A clear developmental framework is therefore required to better understand causal pathways in the development of psychopathologies, as well the timing of individual risk factors that might create vulnerability. Such factors include gestational diabetes, bleeding during pregnancy, or maternal infection, which have been epidemiologically associated with a higher incidence of psychiatric disorders, particularly schizophrenia (SCZ), Autism Spectrum Disorders (ASD), and depression. Early life stress events during neonatal periods and infancy, as well as during critical periods of neurodevelopment (e.g. adolescence) also have a robust impact on the risk for later psychopathology, including exposure to drugs of abuse. The evidence above suggests that the early environment – during fetal, postnatal, and adolescent periods – has a profound effect on mental health outcomes over the life course.

1.2 Strengths

The DRC is a leading centre for studying the impact of early life environmental stressors on brain development conducted by a critical mass of researchers (junior to very senior) with varied and significant expertise.

Key strengths of this TBG:

- **Epigenetic changes.** Our researchers are among the founders of behavioural epigenetics. Since the discovery that epigenetic changes in the brain are linked to experiences and affect the regulation of behaviour, we have continued to show clear leadership in terms of understanding how stress and adversity in early life can affect the development of psychopathology later in life.
- **Whole animal modelling.**
- **Studies in clinical populations.** Longitudinal cohorts looking at mothers and their children (see below), as well as studies examining the impact of environmental disasters during pregnancy have continued to provide insight into the long-term effects of stress on developing children.

The basis behind the creation of this TBG was to consolidate our expertise and to provide a forum for facilitating interactions and collaborations and to maintain our standing as world leaders in the field of early origins of psychopathology.

1.3 Gaps

A comprehensive understanding of the neural mechanisms that underlie the etiology of mental disorders is currently constrained by two critical limitations in science. First, the absence of a developmental framework, and second, an outdated approach to examining the outcomes (i.e., phenotypes) that link genetic or early life environmental risk factors to disease states.

1.4 Strategic objectives

- Determine the impact of early life environmental stressors and drugs of abuse on brain development
- Promote an integrated developmental framework to increase the understanding of the early origins of psychopathology

- Develop innovative, translational, and multidisciplinary approaches to phenotypic analysis of genetic or early life environmental risk factors

1.5 Action plan: achieving our goals in the next 5 years

Through an active scientific program, we aim to promote interactions amongst the different research groups across our institute and the creations of common research platforms, increasing our capacity to develop state-of-the-art translational converging research:

- **Increase our capacity for phenotypic analysis.** Create new phenomics platforms via CFI infrastructure opportunities.
- **Expand the current Douglas animal phenotypic facility** through CFI and provincial funding
- **Increase the engagement of talented trainees.** Provide a stimulating and fertile environment to train the next generation of investigators in the field of the early origins of psychopathology, including regular scientific exchanges (journal clubs, presentations, symposia).
- **Increase research capacity in this area.** Recruiting new and talented principal investigators to this field is critical to maintain the momentum in neurodevelopmental research.

1.6 Major initiatives and partners of this TBG

Maternal adversity, vulnerability, and neurodevelopment (MAVAN)

MAVAN is a project based at the Douglas that follows the effects of parental care (including prenatal care) on the development of children. This project, which is funded by CIHR, is conducted by a team of interdisciplinary researchers across Canada. One of the primary objectives of the study is to clarify the complex relationship between genetics and environment in the context of maternal stress. It also aims to identify effective ways for at-risk women and their babies to adapt to their environment and to encourage positive lifestyle adaptations.

Montreal Antenatal Well-Being Study

The Montreal Antenatal Well-Being Study, which was founded by Douglas Researchers, is one of the largest studies in Canada to explore how biological, social, and psychological factors combine to influence women's mental health and well-being during pregnancy and the postpartum period. One of the main objectives of this study is to understand when the best time is to screen pregnant women for anxiety and depression, and how to effectively improve their mood and mental health during pregnancy and the post-partum period. This project is supported by the *Canada First Research Excellence Fund* and by the *Healthy Brains, Healthy Lives* initiative at McGill.

Ludmer Centre for neuroinformatics and mental health

The Ludmer Centre, which was inaugurated in September 2013, is a one-of-a-kind, multidisciplinary research platform. Its main purpose is to significantly reduce the rate of mental disorders in the population by finding scientific methods of establishing risk factors for disease that appear early in childhood. The Centre integrates diverse branches of research, including neuroscience, computational biology, mathematics, genetics, epigenetics, bioinformatics, epidemiology, and computer science, to analyze large, complex data sets from research projects around the world.

2. Youth mental health and early intervention (Ridha Joober, MD, PhD)

2.1 Need

Youth (12 to 25 years) is a period of immense social, economic, and personal importance. While the foundations of future trajectories of personal growth, social relations and economic productivity are being laid, there is the risk of things going

wrong. The onset of most mental disorders and addictions (75%) occurs during this period, and often persists into adulthood and beyond, especially if not attended to early and effectively. Mental health and addiction (MHA) problems are, therefore, the main obstacle to future productivity, and their contribution to loss of gross domestic product (GDP) is reportedly on par with cardiovascular disorders.

The incidence, prevalence, and distributions of MHA problems are not matched by the current availability and effectiveness of care. It is estimated that 20% of youth experience symptoms of mental disorders and at least 50% of this warrant intervention. The absence or delayed (ranging from months to years) access to adequate services result in poorer clinical and functional outcomes and may also lead to an unknown number of suicides and accidents, especially in specific populations. At the Douglas, we have significantly contributed to the international efforts that have established the effectiveness of early intervention services for psychotic disorders, and we are also among the leaders in extending early interventions to less severe forms of presentations to prevent further decline.

2.2 Strengths

Our group has been at the forefront of innovative approaches to youth mental health research, care and services in psychiatry for nearly two decades, with a commitment to advancing knowledge and improving care for young service users. Key strengths of this TBG:

- **Early intervention services.** The Prevention and Early Intervention Program for Psychoses (PEPP)/ Clinic for Assessment of Youth at Risk (CAYR) are internationally leading and innovative services that function as Learning Health Care Systems, integrating evaluation and research into a high-quality model service. These Early Intervention Services started 18 years ago at the Douglas and have generated unique, new, and innovative knowledge in the field, and have influenced practice in Québec, in the rest of Canada, and internationally.
- **Improving access to care for youth.** The DRC is the host institute for CIHR's largest investment (\$25 Million) in youth mental health services research to date: ACCESS Open Minds (AOM), which has been operating since 2014. AOM is a service model designed through the early intervention research from the DRC that is uniquely adaptable to the immensely diverse communities in Canada, including Indigenous and non-Indigenous communities in urban and non-urban settings.
- **Mobilizing resources to grow research capacity.** Despite the small number of faculty members in the YMH and EI program, they have trained a large number of graduate and post-graduate students, as well as numerous highly skilled research and clinical staff. It is thus an ideal program to attract additional clinical and services research, training, and knowledge transfer funds, and is uniquely positioned to integrate services and research. Through AOM, we are uniquely positioned to have a pan-Canadian platform of research and are seen as leaders in the field.
- **Integration and partnership with clinical and community services.** One of the offshoots of AOM is the creation of a new Youth Mental Health clinical program offering services for youth aged from 0 to 25 years in our CIUSSS. This clinical program is coordinated by Ina Winkelmann, who has over 5 years experience with AOM and is a full member of YMHEI TBG. This cross-appointment is a mechanism that ensures integration of research and care. In addition, Quebec's Ministry of Health and Social Services (MSSS) recently launched the project "Aire ouverte", to build capacity across the province of Quebec in the field of youth mental health services. We have been selected as a pilot site for "Aire ouverte", which will diversify our offer of services and improve the accessibility of care while increasing our capacity to conduct research.

2.3 Gaps

Despite our accomplishments over the last years, a number of challenges remain. In particular, services-based research should be developed further to build on the immense expertise and capacity that is currently held at the DRC. There is an

opportunity, through our close partnership with the CIUSSS, to implement a culture of evaluation and research at all levels of care. While the new Youth Mental Health clinical service offers a horizontal transformation of care (early detection, easy and friendly access to care), there is an additional need to integrate specialized programs to avoid silos of care, promote flexible transitions between levels of care, improve access to high quality treatments, etc. In particular, the Youth Mental Health clinical program needs the buy-in from diverse stakeholders (clinical programs; first, second and third lines of care, community organisation, and youth involvement). Although we have already acquired the expertise needed, we require additional support for this type of research to ensure continued excellence in services and evaluative research.

2.4 Strategic objectives

- Develop an integrated centre for care and research in youth mental health
- Develop strong links between different services and community organizations providing care for youth with developmental disorders and at-risk youth on the one hand, and the Youth Mental Health clinical program, on the other, to recognize and serve the mental health needs of these vulnerable populations.
- Implement MBC across the youth mental health program and ensure a seamless connection with the digital technology. This implementation will also investigate the benefits of MBC on individual outcomes as well as its effect on the efficiency and economy of mental health services.

2.5 Action plan: achieving our goals in the next 5 years

To reach our objectives, we plan to:

- **Collaborate with CIUSSS/Douglas services to create a culture of innovation in service.** Support the integration of research into improved youth services within the CIUSSS ODIM. The resulting synergy will lead to both the DRC and the CIUSSS becoming examples of leadership in services and research. This will be facilitated by the creation of the Centre for Youth Mental Health Service Innovation, Training and Research.
- **Highlight the DRC's expertise in youth mental health research.** Improve administrative support, KT, and communications to highlight the work of DRC researchers for scientific, philanthropic, and broader communities.
- **Contribute to a full implementation of measurement-based care** in the youth mental health programs at the Douglas and the CIUSSS.

2.6 Major initiatives and partners of this TBG

First Episode Psychosis Program (PEPP) and Clinic for Assessment of Youth at Risk (CAYR)

The First Episode Psychosis Program and the Clinic for Assessment of Youth at Risk, respectively, are innovative services and world leaders that function as learning care systems, on a small scale, by integrating evaluation and research in a single service model. The evaluation, intervention, and prevention of psychosis is an integrated clinical, research, and academic program that is based at the Douglas and that offers its services to youth 14-25 who are experiencing their first psychotic episode. PEPP/CAYR is comprised of two essential elements: rapid and simplified access to treatment aimed at reducing delays to treatment and increasing accessibility of care, and an offer of specialized, high quality services that are adapted to the different phases of disease.

Early intervention is based on the hypothesis of a critical period, which underscores the importance of the early stages of disease, and on several studies in the field that suggest that the duration of untreated psychosis has a negative influence on prognosis of disease. Early intervention programs generally last between two and five years, include intensive management and the use of low-dose antipsychotic medication to minimize secondary morbidity. Social functioning, family-

interventions, and attention to related disorders are highlights of these programs, as well as building a therapeutic relationship between youth, the treatment team, and the families. These approaches have shown that early intervention beyond two years is effective. Furthermore, the program for detecting and treating youth who are at high risk of psychotic disorders (CAYR) brings us closer to primary prevention in mental disease. These early intervention services have generated a new approach to building knowledge in the field and its innovative and unique approaches have influenced practices in Quebec, in Canada, and internationally.

ACCESS-Open Minds

ACCESS-Open Minds is a partner of this theme-based group and is an unprecedented five-year research project aimed at improving the quality and speed of mental health services for young people aged 11 to 25. It is a transformational model of care that could later be replicated across the country. The Douglas Research Center is the host site for this unprecedented investment (\$ 25M) from CIHR in youth mental health and has been governing one of the 14 ACCESS-Open Minds project sites since 2014. This service model, established through research on early intervention that was conducted at the Douglas Research Center (PEPP-Montreal), has a unique flexibility that allows it to be implemented across various communities in Canada, including Indigenous communities, in urban and non-urban settings.

Youth Mental Health Program (0-25 years):

This program has been created recently and important efforts are being deployed to create the pathways to care, to facilitate access to services and to implement a larger research program in this population, including at-risk youth (with developmental disorders, under the youth protections, homeless youth, etc.).

Eating Disorders Continuum

The Eating Disorders Continuum (EDC) is the most developed program in Quebec for adolescents and adults on the eating disorders (ED) spectrum, including anorexia nervosa, bulimia, and related disorders. The EDC has a supra-regional mandate and is the cornerstone of the care offered to Quebecers with EDs, acting as a centre of clinical and research expertise. Thanks to a continuum across levels of specialized care and across the life cycle, the EDC is the only program in Quebec to offer complete, uninterrupted care at all stages of recovery, and for all ages. The EDC offers cutting-edge treatments, conducts clinical research to guide new curative and preventive treatments, and trains professionals from various sectors of the health network and academia. Considered by many to be the best ED program in Canada, its research program is internationally recognized. In addition, its researchers have published hundreds of scientific articles and are regularly invited to present their research results on the international stage. Since 2009, EDC has also offered a very successful and award-winning supra-regional knowledge exchange program that links the EDC's specialized services to community services in many regions of Quebec. In this program, the EDC's specialized staff provides training to community clinicians on the assessment and treatment of EDs, to enable people living in several regions of the province to quickly access informed and effective care in their region. The EDC is closely connected to the Youth Mental Health clinical program, which will improve accessibility of care to the 0-25 population of patients and a diversity of environments where care can be provided.

Connection with other TBGs and research divisions:

Although innovation in service research is at the center of our interests, the group of researchers with primary affiliation to this TBG bring various skills and technical tools of investigations (qualitative, quantitative and economic analyses; genetics, sophisticated brain imaging techniques, e-mental health), the links between this TBG and other TBGs, particularly the "Environmental Adversity, Neurodevelopment, and Mental Health" are organic and highly synergetic. Many researchers from the various clinical divisions (particularly clinical and human neuroscience divisions) are part of this TBG. This is a strong

reflection of our commitment to make youth mental health not only a research project the fruits of which are awaited, but also a true reality in the lives of our youth and their families.

3. Aging, cognition, and Alzheimer's disease (Pedro Rosa-Neto, MD, PhD)

3.1 Need

Currently, age-related neurodegenerative diseases affect 10% of individuals 65 and over, and 30% of those who are 85 and over, and Alzheimer's disease (AD) constitutes the chronic disease that worries seniors the most. To prevent these conditions, it is crucial to advance research and care in aging health and cognition. Progress in basic sciences, biomarker technologies, and genetics provided unprecedented insights regarding basic mechanisms and disease pathophysiology in humans. Despite the significant progress of the past 30 years, a considerable number of gaps prevent the development of optimal therapies capable of treating or preventing neurodegenerative conditions in the elderly. The study of age-related cognitive disorders has become increasingly multidisciplinary to better address these gaps. Better animal models are necessary to investigate the complex mechanisms underlying the cognitive deficits that occur as part of the neurodegenerative process. In clinical research, better biomarkers and pathophysiological characterization of patients is needed to diagnose and assess the efficacy of disease-modifying interventions. Novel clinical trials aiming to mitigate disease pathophysiology are crucial for the preventing dementia. Finally, in the context of the ongoing pandemic, research involving clinical populations must contend with the additional challenge of remote assessment of behaviour, biomarkers, genetic stratification, and sex differences necessary for personalizing care and dementia prevention.

3.2 Strengths

The Aging, Cognition, and Alzheimer's Disease theme-based group (ACA-TBG) comprises a multidisciplinary group of scientists from clinical and neuroscience divisions of the DRC, the Centre for Studies on the Prevention of Alzheimer's Disease (StoP-AD), and from the McGill Centre for Studies in Aging (MCSA). The ACA-TBG includes two highly regarded basic research scientists with cutting-edge expertise in the modelling and animal neurophysiology of the pathophysiology of Alzheimer's disease.

Key strengths of this TBG:

- **Primate investigation unit.** Brandon and Williams have set up and are leading the behavioural component of McGill's new primate investigation unit; they also introduced new, highly sophisticated behavioural analysis methods to examine the neural circuits underlying behavioural and cognitive consequences of ageing.
- **Animal imaging.** Chakravarty has implemented cutting-edge neurophenotyping using functional and structural MRI.
- **Aging cohorts.** Another major strength of the ACA-TBG is to design and implemented highly specialized aging cohorts. The DRC has three large, extensively phenotyped, longitudinal, observational cohorts focusing aging and Alzheimer's disease. One includes middle-aged individuals with risk factors for Alzheimer's disease and explores the influence of sex, gender, and social determinants of health (Rajah) and two focus on seniors who are either at risk of developing Alzheimer's disease (Villeneuve, Poirier, Breitner) or who are already symptomatic (Rosa-Neto). Ducharme, who recently has joined the DRC, has started original cohorts on frontotemporal dementia.
- **Brain banking.** The collection of aging and dementia brains at the DBCBB is a major asset, with a vast collection of well-characterized brain specimens, including genetic cases of AD and atypical dementias.
- **Clinical trials.** The research conducted in these cohorts synergizes with pharmacological therapeutic clinical trials conducted in the Douglas Memory Clinic (Nair, Ducharme, Rosa-Neto) as well as the StoP-AD (Villeneuve, Poirier, Breitner) and MCSA (Gauthier, Rosa-Neto) or non-pharmacological therapeutic clinical trials focusing on Meditation (Nair), cognitive stimulation (Bohbot) and lifestyle interventions (Villeneuve, Poirier, Breitner, Chakravarty).

- **Scientific productivity.** The ACA-TBG has a highly productive and impactful scientific presence nationally and internationally, ranking among the top three in Canada (along with UBC and UofT). As a community, the ACA-TBG scientists have jointly published several articles and book chapters.
- **Knowledge translation.** Members of the ACA-TBG are highly engaged in KT activities. For example, Gauthier and Poirier authored *“La Maladie d'Alzheimer: diagnostic, traitement, recherche, prévention”* for the lay public. Gauthier and Rosa-Neto have been commissioned to write the World Alzheimer's Reports from *Alzheimer's Disease International* for 2021 and 2022, which is targeted toward patients and dementia associations. Gauthier and Rosa-Neto also edited the Case studies published by Cambridge University (2014, 2021). Gauthier, Poirier, Villeneuve, Chakravarty and Bohbot are very active on the lay press.
- **Inclusion.** Rajah chairs the DRC the Equity, Diversity, and Inclusion Committee on behalf of the four research divisions.
- **Open Science.** Villeneuve and Poirier have accomplished important steps towards open science with the StoP-AD cohort. They have started to make the results of our research in prevention of Alzheimer's disease available (without restriction) to scientists around the world. These open data include PET imaging, magnetic resonance imaging, comprehensive measures of cognition, blood and brain biomarkers as well as several genetic markers. Access to the enormous amount of data accumulated over the past 9 years as part of our PREVENT-AD program is now available to the entire international community.

The ACA-TBG (previously represented through the ageing axis) has a long tradition of excellence, having received a ranking of "exceptional" by the FRQS Evaluation Committees for FRQS Research Centres in the last three renewals of the Research Centre (over the previous 16 or more years).

3.3 Gaps

As methodologies and technology evolve, we will need to address several emerging gaps to maintain our leadership position in aging, cognition and Alzheimer's disease research. First, new models for disease need to be adopted to improve translation of findings from models to humans. To fully explore the complex brain mechanisms of aging and cognition, experiments must be conducted in non-human primates. Due to their biological proximity to humans, marmosets (*Callithrix jacchus*) have emerged as a novel animal model that is particularly well-suited to biomedical and neuroscience research. Therefore, a primate animal facility constitutes an infrastructural need to achieve leadership in aging neuroscience. Second, ACA-TBG members have been heavily engaged in biomarker research, yet will not be able to establish themselves at the forefront of biomarker discovery until several organizational and infrastructure-related barriers have been overcome. Third, targeted recruitments will be required to maintain the research capacity necessary to continue to be leaders in aging research.

3.4 Strategic objectives

- Advance the neuroscience research in aging by incorporating non-human primate models (marmosets), to examine the behavioural and cognitive consequences of aging, as well as the effects of introducing genetic factors linked to Alzheimer's disease.
- Advance biomarker research by establishing a central biobank and a central biomarker analysis infrastructure
- Harmonize cognitive, clinical, and behavioural assessments across DRC cohorts and build a data lake by establishing harmonized cognitive, clinical, and behavioural assessments across clinical populations
- Expand the Open Science aspect of our research in collaboration with the Canadian Open Neuroscience Platform

3.5 Action plan: achieving our goals in the next 5 years

- **Design and implement a primate animal facility.** This facility will be fully integrated with the DRC neuroinformatics resources that are being created to facilitate databasing and subsequent data sharing.
- **Create optimal conditions for biomarker research in Alzheimer's disease.**
 1. *Create a common clinical area for patient assessment and collection of samples (central biospecimen bank with wet laboratory spaces, centralized freezers, and a dedicated management system). This is crucial for sample curation and storage.*
 2. *Develop a core platform for fluid biomarkers. Currently, several members of the ACA-TBG rely on international collaborations to conduct research on fluid biomarkers; having a core platform for fluid biomarkers at the DRC would tremendously accelerate biomarker discovery and validation at the ACA-TBG.*
 3. *Harmonize human behavioural and cognitive data collection within the DRC cohorts.*
- **Recruitment.** To remain competitive, the ACA-TBG will require targeted recruitment. We plan to recruit:
 1. *A scientist with expertise in neuroinformatics to move forward with data analysis and open science.*
 2. *A clinician-scientist specialized in aging to better connect clinical services to research in aging.*
- **Integrate research data in aging research.** The integration between central biospecimens bank, a core platform for fluid biomarkers, and human behavioural and cognitive data collection, and the DRC neuroinformatic infrastructure (see above) would allow unprecedented analytical possibilities within the institution as well as in the context of open science.

3.6 Major initiatives and partners of this TBG

McGill Centre for Studies on Aging

Located at the Douglas Institute, the McGill Centre for Studies in Aging brings together researchers from the Douglas and other McGill network research centres. The MCSA has the translational biomarker for aging and dementia (TRIAD) cohort. The MCSA runs a memory clinic (MCSA Clinic) and uses advanced techniques to analyze healthy brains and those affected by pathological conditions associated with dementia. The unit conduct trials in specialized populations such as genetic forms of Alzheimer's disease.

Moe-Levin and Memory Clinic (a CIUSSS-ODIM clinic)

This program provides geriatric psychiatry services across the neurocognitive disease spectrum. It includes an outpatient memory clinic with over 3500 visits/year, a day program, a behavioural and psychological symptoms of dementia outreach team serving several long-term care nursing homes and an inpatient 18 beds unit specialized in the treatment of behavioural and psychological symptoms of dementia. The Moe Levin Therapeutic Day Centre currently serves people with mild to moderate cognitive deficits in order to maximize their cognitive and social skills and delay placement. It provides a therapeutic environment for people living with cognitive deficits and dementia-related symptoms with multiple therapeutic activities. The Therapeutic Day Centre has a strong knowledge transfer program specially design to assist caregivers and families to understand and manage dementia-related symptoms. The unit conduct pharmacological and non-pharmacological trials in dementia populations.

Centre for Studies on Prevention of Alzheimer's Disease (StoP-AD)

The scientific mandates of the Centre for Studies on Prevention of Alzheimer's Disease are, firstly, to identify the biological determinants responsible for the development of Alzheimer's disease in its asymptomatic phase in people at risk who are cognitively normal and, secondly, to evaluate effective preventive approaches that could modify the trajectory of the disease and alter the identified biological determinants. StoP-AD maintains and characterizes the cohort of more than 425 asymptomatic subjects with a parental history of Alzheimer's (PREVENT-AD cohort) in order to identify the biological determinants associated with the onset of Alzheimer's disease (neuroimaging, cerebrospinal fluid and blood samples, genetic determinants of risk/protection by GWAS, sensory or cognitive determinants). In addition, StoP-AD is conducting clinical trials of pharmacological agents capable of modulating biological determinants by reducing risk factors or by stimulating protective factors.

StoP-AD resources include:

- Stop-AD open-science biomarker research platform
- Open web platform for human neuroscience (based at the MNI and in Europe)

Additional resources part of the ACA-TBG

- A large brain imaging program (MRI at the Douglas and PET at the MNI)
- A program focused on animal MRI scanners (Douglas)

Canadian Consortium on Neurodegeneration in Aging (partner)

Several of our researchers are theme or platform leaders involved in the Canadian Consortium on Neurodegenerative Diseases Related to Aging (CCNA). This includes Drs. Rosa-Neto (Co-chair of inflammation theme), and Poirier (Chair of the CSF biomarkers platform), who are two of the co-principal investigators of the \$32M CCNA consortium. Rajah and Bohbot (Cognitive Intervention, Reserve and Brain Plasticity), Villeneuve and Chakravarty (Developing New Biomarkers), and Ducharme (Frontotemporal Dementia) Breitner (inflammation theme) are also CCNA members.

Canadian Open Neuroscience Platform (partner)

The Canadian Open Neuroscience Platform (CONP) aims to build an interactive network of collaborations in brain research enabling interinstitutional infrastructure for sharing of both data and methods. CONP aims to remove the technical barriers to practicing open science and to improve the accessibility and reusability of neuroscience research to accelerate the pace of discovery.

Quebec Research Network on Aging (partner)

The mission of the Quebec Research Network on Aging (QRNA) is to support interdisciplinary and interuniversity research on aging, based on a variety of methodological approaches. All ACA-TBG researchers are affiliated to the QRNA.

Other key affiliations

Our researchers are members of national and international consortia: ADRC DIAN (USA), ADCS (USA), ADNI (USA), CCNA (Canada), CIMA-Q (Quebec), C5R (Canada) and BIOMARKAPD (European).

4. Sleep and biological rhythms (Nicolas Cermakian, PhD)

4.1 Need

Most psychiatric and neurodegenerative diseases are associated with disturbed circadian rhythms and sleep-wake cycles, including mood disorders, ADHD, eating disorders, autism, schizophrenia, Alzheimer's disease, multiple sclerosis, and Parkinson's disease. Similarly, work on atypical schedules increases the risk of various medical and psychiatric conditions.

Therefore, circadian and sleep disruption are increasingly considered as significant risk factors for the development or aggravation of mental disorders. Research on sleep, circadian rhythms, and other biological rhythms is in an exciting and expanding period, and the DRC is in position to assume a leadership role in this field. Current research has begun to address how improving daily rhythms and the sleep-wake cycle could prevent onset of disease, help treat these conditions, or promote cognitive and mental health. Thus, disruption of circadian rhythms and sleep are core aspects of most mental disorders, impacting cognitive, emotional, and behavioural functioning, and are involved in the pathophysiology of mental disorders. Given the prevalence of sleep/wake and circadian disturbances in modern societies, and their resulting negative consequences, this field of research addresses important public health issues. This has significant implications for individualized health, clinical practice, public health, and society. In sum, a general objective is to consider circadian rhythms and sleep in the prevention and treatment of mental disorders, and ultimately to enhance physical and mental wellbeing, cognition, and daytime functioning of different target populations.

4.2 Strengths

The Group for Sleep and Biological Rhythms has recently emerged as a group of internationally leading experts in the fields of sleep and chronobiology. Group members study the implications of biological rhythm/sleep disruption and regulation in various diseases including mental disorders through human, basic, and translational research.

Their work includes studies on patients with primary circadian rhythm disorders or psychiatric disorders characterized by a high prevalence of disrupted sleep or eating patterns, clinical implications of living on atypical schedules such as what occurs in shift work, the interplay between youth sleep, health, and cognition, innovative strategies using sleep improvement to enhance youth physical and mental health and daytime functioning, and epidemiology and clinical trials to correct sleep and rhythm disruptions.

Key strengths of this TBG:

- **Cohesive, collaborative research group.** Sleep and chronobiology research at the Douglas have a history of successful collaboration, producing high-quality translational research, with many joint articles and grants.
- **Focus on creating a high-quality training environment.** This integrated approach to research has helped to teach and train the next generation of sleep and biological rhythms specialists, an expertise that is increasingly sought after in academia, clinic, and in the private sector.
- **Presence of specialized infrastructure.** Dedicated equipment and infrastructures are essential to the activities of this group. These include equipment to record bioluminescence and molecular rhythms in animal tissue explants, human samples, and cell lines; infrastructure to monitor activity rhythms of rodents, and cellular ultradian and circadian rhythms in the brain of live rodents; accommodation suites with controlled light and isolation from external time cues for assessing various physiological rhythms in human subjects; and infrastructure to measure/integrate neuropsychological, behavioural, and neurophysiological outcomes following experimental changes in sleep patterns.

4.3 Gaps

Although some translational research involving basic and applied research laboratories already occurs at the Douglas, we need to expand this to truly integrate clinical research and practice on circadian rhythms and sleep. Stronger links with clinical services (CIUSSS) must be developed to fully integrate research and clinical protocols. Additionally, we require state-of-the-art eHealth/artificial intelligence expertise to study biological rhythms in vulnerable populations. Finally, we are missing expertise in the study of sleep mechanisms and how they explain sleep phenotypes in rodent models of psychiatric diseases.

4.4 Strategic objectives

- Expand translational research to truly integrate clinical research and practice on circadian rhythms and sleep
- Design innovative approaches to promote sleep health and to study and treat circadian rhythm and sleep disruption in populations at risk of developing sleep and circadian rhythm disorders
- Develop research capacity to further strengthen this emerging TBG

4.5 Action plan: achieving our goals in the next 5 years

These objectives will be addressed using the following strategies:

- **Recruit strategic candidates to address gaps in expertise:**
 1. *Clinical and developmental sleep research* combined with implementation of medical intervention and health psychology, in healthy and clinical populations;
 2. *Translational intervention studies* in relation to sleep and circadian rhythms, with a focus on both medical and non-medical treatments;
 3. *Computational biology, eHealth and artificial intelligence* applied to biological rhythms, e.g. using modern AI and data handling approaches to use large-scale datasets (including from population-based studies related to sleep and circadian rhythms in vulnerable populations) to identify new biomarkers for circadian rhythms and sleep;
 4. *Sleep neuroscience*, e.g. a researcher using animal models to identify new molecular components and/or brain networks involved in sleep-wake regulation and disrupted in mental disorders.
- **Create clinical programs on sleep and circadian rhythms that include strong research objectives.** Recruit clinician-scientists with funding and facilities to conduct clinical research and practice on circadian rhythms and sleep and promote evidence-based sleep interventions in psychiatric care.
- **Develop research efforts focused on mechanistic links between mental health and illness and sleep/biological rhythms**, at the molecular, cellular, physiological, behavioural and clinical levels throughout development and adulthood. One of the approaches towards this will be the creation of new meeting and networking opportunities, allowing exchange of ideas and fostering new interdisciplinary collaborations, while giving opportunities to students to present their work. Seminars and special symposia on circadian rhythms and sleep will also be organized.
- **Expand and diversify chronobiology and sleep facilities**, including by capitalizing on opportunities such as NSERC RTI and CFI. Such facilities will include high-resolution cellular and physiological studies in live animals and ex vivo cultures, development of equipment for ambulatory investigation of sleep and circadian rhythms in humans, and integrated clinical research facilities for the study and treatment of human sleep and circadian rhythms disorders.
- **Develop a strong translational training environment** for students to study circadian rhythms and sleep. In addition to the new meetings and networking aspects described above, this item will be pursued via the co-supervision of trainees to provide multi-disciplinary training, as well as opportunities for team or training grants, with colleagues of other institutions.

5. Stress, anxiety, depression, and suicide (Naguib Mechawar, PhD)

5.1 Need

Stress is a well-known precipitating factor for various health problems. It is particularly associated with mental disorders such as mood, anxiety, and eating disorders, which are all strongly associated with suicide, itself the cause of more than

800,000 deaths each year. Depression alone is the leading cause of disability worldwide, and mood, anxiety, and eating disorders account for more than 15% of disability-adjusted life years lost. Increasing our research capacity on stress and these mental disorders is clearly a priority if we are to reduce their impact on society. In particular, there is an urgent need for pre-clinical and clinical investigations aimed at deciphering stress-associated molecular mechanisms and identifying novel biomarkers and therapeutic strategies.

5.2 Strengths

There is a rich tradition at the DRC of investigating stress (across the lifespan) and the impact it can have on mental health, and the inclusion of renowned experts on bipolar disorder, anxiety and trauma, and animal models of resilience, stress, and related disorders, widens its scope while increasing its focus.

Key strengths of this TBG:

- **Early-life stress and mood disorders.** Using a variety of approaches, from basic models to the clinic, we have developed a particular strength in early-life stress and mood disorders research. The Stress, Anxiety, Depression, and Suicide (SADS) TBG is notably composed of members of the McGill Group for Suicide Studies (MGSS; 7 primary affiliates: Berlim, Chachamovich, Geoffroy, Mechawar, Renaud, Richard-Devantoy, Turecki). The MGSS adopts varied approaches to investigate the biopsychosocial underpinnings of depression and suicide, in view of improving prevention and treatment strategies.
- **Bipolar disorder.** (Beaulieu)
- **Anxiety and trauma disorders.** (Brunet)
- **Animal models of molecular/cellular/network aspects of stress, resilience, and stress-related disorders.** (El Mestikawy, Giros, Gratton, Rochford, Wong)

This unique combination of expertise and approaches benefits from access to shared DRC platforms, such as the animal facility and Neurophenotyping Centre, Brain Imaging Centre (human and small animal brain scanning), the Douglas-Bell Canada Brain Bank (DBCBB), the Molecular and Cellular Microscopy Platform (MCMP) and the Platform on Biopsychosocial Analyses of Mental Health Trajectories.

5.3 Gaps

A key gap is the need to increase translational research on stress and stress-related mental disorders. To achieve this, we must strengthen our pre-clinical (fundamental) research on animal models of depression and anxiety, and related phenotypes. Additionally, we must facilitate the establishment of clinical investigations that are better informed by such (and other) studies. Research should also better exploit to their full potential the possibilities offered by DRC platforms and the availability of patient populations in our CIUSSS.

5.4 Strategic objectives

- Decipher stress-associated molecular mechanisms and identifying novel biomarkers and therapeutic strategies
- Strengthen our pre-clinical research on animal models of depression, anxiety, and related cognitive deficits
- Expand on current randomized control trials aimed at stress reduction

5.5 Action plan: achieving our goals in the next 5 years

To meet our objectives, we will:

- **Recruit an animal model specialist.** This recruit will specialize in using cutting-edge molecular and behavioural approaches to study basic mechanisms associated with depressive and anxiety related phenotypes.
- **Modernize the research instruments in our heavily used platforms.**

- **Establish participant/patient cohorts through DRC/CIUSSS clinical programs** to increase clinical and translational research activities. Longitudinal cohort/clinical studies should be designed to implicate as many of our TBG members as possible (biomarker studies, neuroimaging, post-mortem research, models based on cohort findings, etc.).
- **Expand on current randomized control trials** aimed at stress reduction.

5.6 Major initiatives and partners of this TBG

Centre for Breakthroughs in Teen Depression and Suicide Prevention

The Centre for Breakthroughs in Teen Depression and Suicide Prevention aims to improve access to mental health services for youth and evaluate the efficiency of treatments and prevention approaches in depression and suicide among Canadian teens. The goal is not to add intervention approaches, but rather to establish, through scientific methods, which existing approaches are effective for preventing depression and suicide among teens. Building on these findings, the Centre aims to determine how these interventions, treatments, or therapies might benefit other networks and thereby contribute to an overall reduction of the incidence of depression and suicide in teens.

Centre for Translational Research on Mood Disorders and Suicide

The Centre for Translational Research on Mood Disorders and Suicide, which was established in 2015, combines several research areas – clinical, neuroanatomy, molecular and cellular biology, and epigenetics – with the goal of understanding the mechanisms underlying mood disorders and suicide. The Centre is fully equipped with the tools to conduct translational research, a form of research that allows knowledge developed in basic and clinical research to be applied directly to patient. The laboratory facilities are fully furnished with state-of-the-art instruments dedicated to the study of post-mortem brain tissue (histology), cellular and tissue imaging, and the cellular culture of human brain tissue. The Centre also benefits from a unique combination of cutting-edge platforms at the Douglas including the Douglas-Bell Canada Brain Bank and the Brain Imaging Centre. It is the first Centre of its kind in Canada to dedicate itself to this area of study and offers the additional advantage of integrating neurobiological research into clinical practice, with the Depressive Disorders Program, with which it is affiliated.

The McGill Group for Suicide Studies (MGSS)

The MGSS focuses its activities on the study of risk factors that are associated with suicidal behaviour and associated disorders. This multidisciplinary team is unique in Canada and is one of the only services of its type in the world. Its goal is to understand what predisposes individuals to suicide, using different research strategies that are based on the study of brain tissue, the genome, and on clinical and social environmental factors to understand what happens in the brains of individuals before they die by suicide.

Measuring Our Progress

Short-term indicators

1. **Strategic Goal: Improving translational approaches in research**
 - Participation in joint committees with CIUSSS
 - Joint framework/policy documents/projects pursued
 - Targeted recruitment procedures initiated
 - TBG-based initiatives
2. **Strategic Goal: Increasing overall DRC funding**
 - Success rate in major grant competitions
 - Financial support for research infrastructures
 - Number of industry partnerships
 - Financial contributions from private sector (industry and donor)
3. **Strategic Goal: Increase provincial, national & international outreach**
 - Complementary training initiatives (number, diversity, participation of trainees)
 - External recognition of success/innovation (prizes to faculty and students)
4. **Strategic Goal: Modernizing our approaches to research**
 - Availability and activity of shared resources
 - Usage of research infrastructures (number of users, number of publications, variety of user types)

Medium-term indicators

1. **Strategic Goal: Improving translational approaches in research**
 - Cohesive and complementary approaches to DRC activities – publications per TBG, multi-PI collaborations
 - Reinforced research capacity around targeted research areas – grants secured per TBG
 - Implementation of innovations developed by our researchers into the CIUSSS clinical programs
2. **Strategic Goal: Increasing overall DRC funding**
 - Funding leveraged from external sources
 - Variety of sources, dollar amount, synergy with Douglas Foundation to attract major gifts
3. **Strategic Goal: Increase provincial, national & international outreach**
 - International collaborations
 - Integration of knowledge in practice and development of policies
 - Number and type of exchanges with general public
 - Exchanges and interactions with policy decision makers

4. Strategic Goal: Modernizing our approaches to research

- Infrastructure funding
- Shared digital infrastructures for the DRC

Long-term indicators

1. Strategic Goal: Improving translational approaches in research

- National and international leadership in mental health research
- Number of publications explicitly citing the DRC
- Impact of publications (transformation of research approaches and clinical/public health practice)
- Implementation of innovations developed by our researchers into provincial and national healthcare environments

2. Strategic Goal: Increasing overall DRC funding

- Total DRC revenue
- Distribution of funding between grants, industry, and donations

3. Strategic Goal: Increase provincial, national & international outreach

- International recognition of our expertise

4. Strategic Goal: Modernizing our approaches to research

- New Research Centre with state-of-the-art capabilities
- Creation of digital solutions in neuroscience and psychiatry research

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