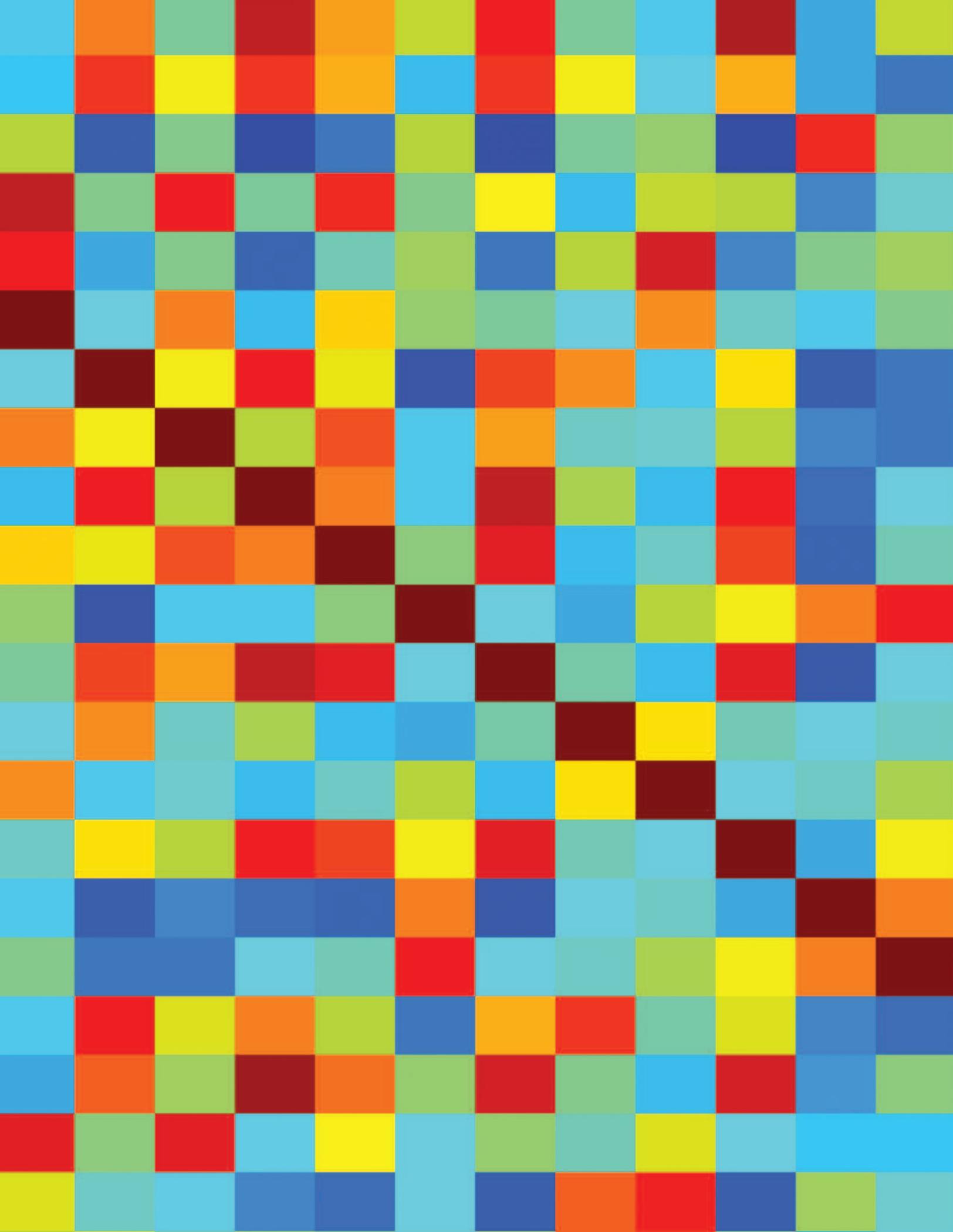


The Ontario Brain Institute

A Proposal to Mobilize Ontario's **Excellence** in Brain Research

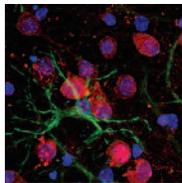


THE ONTARIO BRAIN INSTITUTE
A Proposal to Mobilize Ontario's
Excellence in Brain Research

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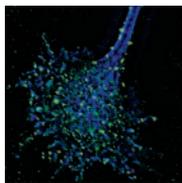
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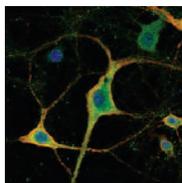


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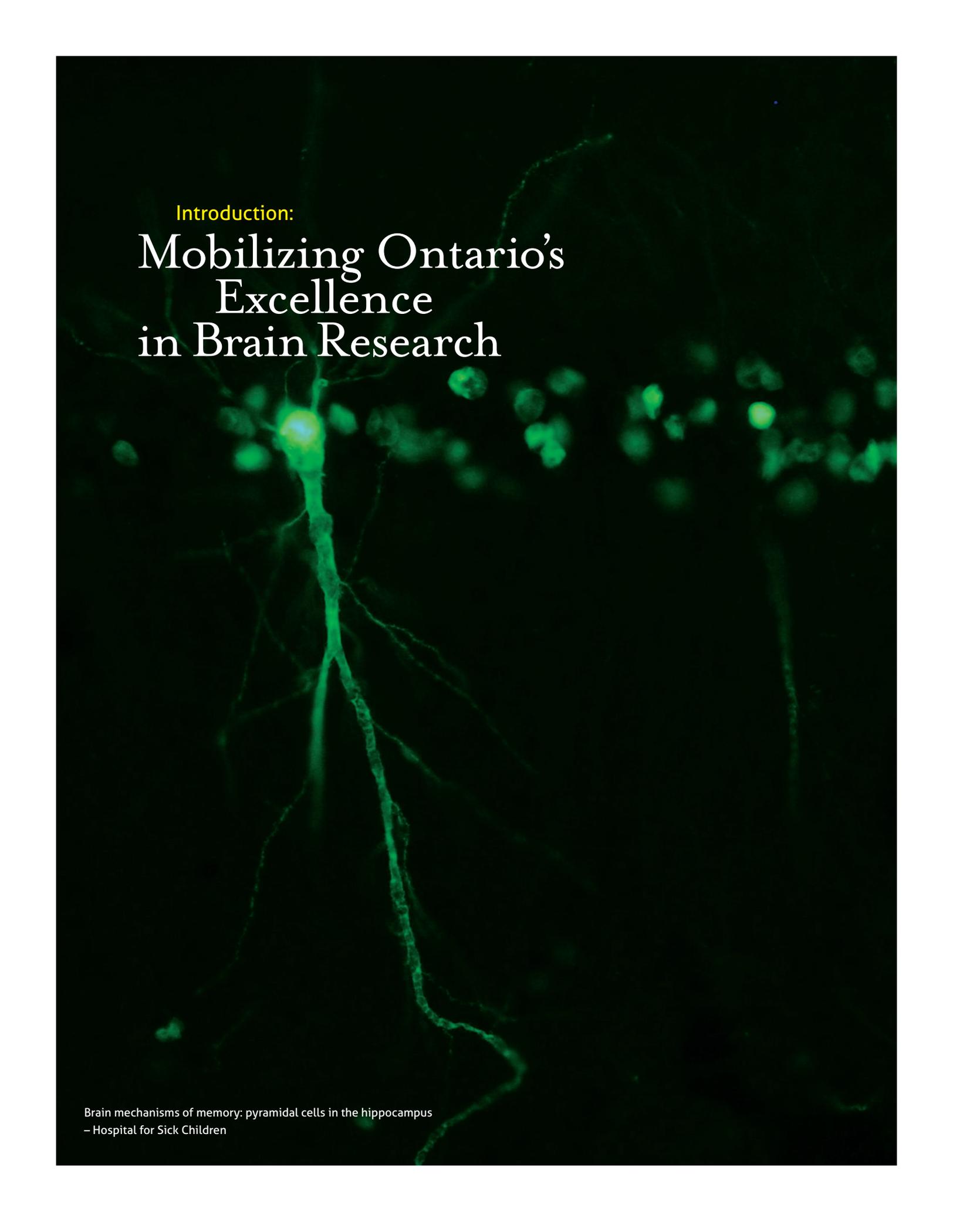
The Century of The Brain

Early in 2009, groups of world-leading neuroscience researchers from top universities and research centres in Canada, Great Britain, Europe, and the United States, along with Canadian industry leaders, met separately and together in Toronto. Led by eminent Canadians Dr. Joseph B. Martin, Dean Emeritus, Harvard Medical School, Joseph L. Rotman, businessman and philanthropist, Dr. Fergus Craik, Professor at the University of Toronto and Rotman Research Institute, and Dr. Richard Murphy, President and CEO of Salk Institute for Biological Studies (retired), these experts set out to explore whether Ontario could play a leadership role in the burgeoning field of neuroscience.

The subject was pressing and the moment timely, for recent advances in brain research have brought us to the very threshold of developing treatments — and potential cures — for diseases and disorders of the brain that have plagued humankind for centuries. Indeed, due to the fast pace and breakthrough nature of neuroscience research, this century has been dubbed **“The Century of the Brain”**. And governments, universities, and foundations worldwide have marshaled enormous talent and resources to drive this critical research forward.

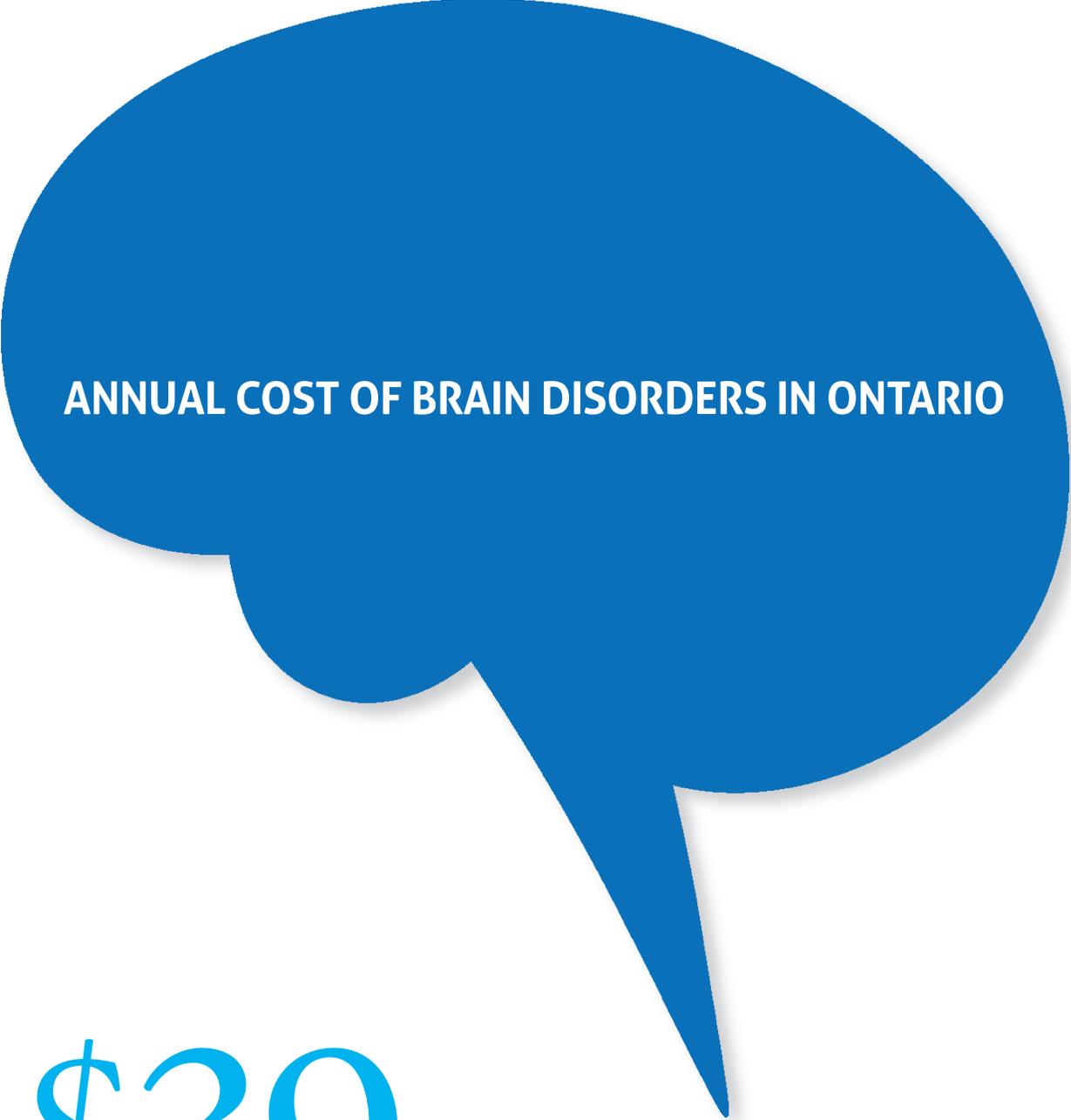
What strengths could Ontario bring to the international effort? And, within the complex worlds of clinical and basic neuroscience, could Ontario become a world leader in discovering new knowledge about the brain, applying it to the care of patients afflicted with brain diseases, and commercializing it to create new wealth?

The findings and recommendations of our experts in exploring these questions are detailed in this report. They conclude that Ontario can indeed be a global leader in neuroscience — for the benefit of Canadians and people worldwide.

A fluorescence micrograph showing a network of neurons. A prominent neuron in the center-left has a bright green soma and a long, thin dendrite extending downwards. Other smaller green spots are scattered in the background. The overall image is dark with green highlights.

Introduction:
Mobilizing Ontario's
Excellence
in Brain Research

Brain mechanisms of memory: pyramidal cells in the hippocampus
– Hospital for Sick Children



ANNUAL COST OF BRAIN DISORDERS IN ONTARIO

\$39 BILLION

ESTIMATED IMPACT OF BRAIN DISEASES AND DISORDERS ON ONTARIO'S ECONOMY

Introduction:

MOBILIZING ONTARIO'S EXCELLENCE IN BRAIN RESEARCH

Diseases and disorders of the brain impose huge medical and social burdens on the daily lives of patients and their families across the world. In Canada, one in four citizens will suffer from a brain disease sometime over their lifetime, a statistic with enormous implications for the cost of care, reduced productivity, payments for long-term disability, and, of course, quality of life. In Ontario, brain-related diseases cost mightily — an estimated \$39 billion annually.¹ Even this figure is likely conservative given the stigma attached to disclosure of mental illness by employees.

No age group is spared the devastation of brain diseases. Children with autism, learning disabilities, and other neurological problems have enormous hurdles to overcome during their crucial, formative early years of life. Young people showing the first signs of mental disease suffer innumerable problems, including societal stigmas, which have long-term effects on their ability to function well in society. Adolescents and young adults who have suffered head injuries have high risks of depression and stress syndromes. Adults with mental diseases are frequently unable to hold jobs and care for themselves, which too often leads to addiction, homelessness, and crime. Brain injury due to stroke and debilitating seizures arising from epilepsy, as well as neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, and multiple sclerosis steal from their victims productive years of life and happiness while imposing tremendous care burdens on their families and society.

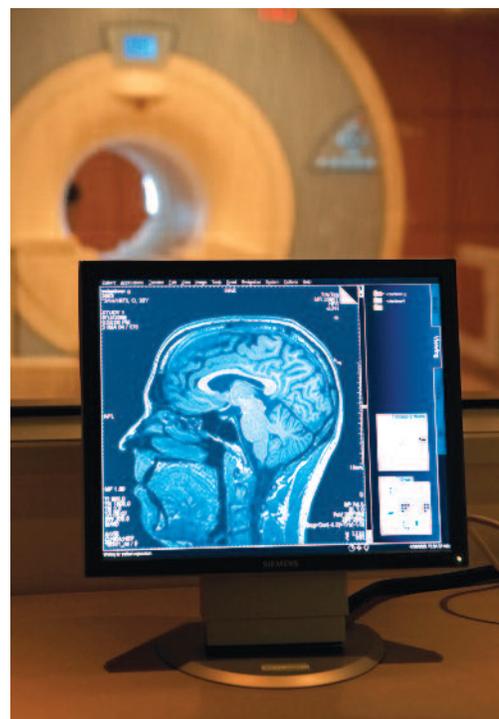
The unfortunate truth is, while some brain diseases respond to treatment, there are no cures at the present time. The medical profession simply lacks fundamental information about how the human brain functions as a controlling organ of the body. We still do not understand fully how nerve cells and the cells that support them work within the brain, how information is processed, and what causes major brain diseases. Without this knowledge, creating therapies to prevent and effectively treat brain diseases is impossible.

However, we now have optimism.

Today, for the first time in the history of mankind, scientists stand on the threshold of understanding how the human brain works — a revolution in knowledge that even 20 years ago was unthinkable. This capacity to understand the brain stems from major advances in technology that have allowed the organ to be investigated in ways never before possible.

For example:

- Functional magnetic resonance imaging (fMRI) now permits us to visualize — within living people — brain regions that gather and interpret information, generate responses, and create and process emotions. *(see image on right)*



Courtesy of Rotman Research Institute

- The genome project, having identified all genes in the cells of the human body, has enabled us to identify single-gene abnormalities that dysregulate nerve cell physiology and cause certain brain diseases.
- High-throughput methods of genome-wide sequencing are allowing scientists to investigate entire patient populations in a quest to identify cohorts of genes responsible for complex brain disorders, including mental diseases.
- Genetic studies have allowed scientists to create models of human brain diseases in experimental animals by adding, subtracting, and mutating genes, making the models amenable to testing new drugs.
- Deep brain stimulation has succeeded in reducing tremors in Parkinson's disease patients, in alleviating the symptoms of treatment-resistant depression, and in improving memory within certain patient populations.
- Methods are now available to identify, track, and modulate the activity of single nerve cells within the brain, permitting study of their connections and roles in normal brain function and disease.
- Major advances have been made in understanding the chemicals that drive nerve cells, including, for example, membrane channels that regulate electrical activity and the cellular proteins that lead to Alzheimer's disease, Parkinson's disease, and Lou Gehrig's disease.
- The brain, once thought to be hard-wired and immutable, is now known to rearrange synaptic connections between nerve cells to create and store memories, and to adjust to environmental factors.
- Recent discoveries show that brain stem cells not only repair the brain following injury, but also replenish nerve cells in the course of daily living.

Scientists across the globe are recognizing the potential of these and other advances to open avenues in our understanding of how the brain functions — and to use this new knowledge to alleviate human suffering. Spurred on by enormous, recent gains, the governments of developed countries have begun making major investments in brain research, as have philanthropic foundations and disease-based charitable organizations worldwide. The goal of these investments is to expand the quantity and quality of brain research within specific jurisdictions, to foster interdisciplinary collaborations among scientists working in diverse disciplines, and to overcome the artificial barriers that until now have separated basic scientists, who labour to understand how the brain works, from clinical scientists and physicians, who treat patients suffering from brain diseases. These investments are also expected to yield commercial outcomes that contribute to the economy as well as to the needs of patients.

Ontario, thanks to its intellectual assets, is a player in this international revolution in brain research. The province's universities and their affiliated hospital research institutes are recognized as centres of excellence in basic neuroscience research as well as in the medical disciplines that deal with clinical neuroscience, including neurosurgery, neurology, psychiatry, and psychology. Ontario-based academic scientists are among the world's experts in functional brain imaging, deep brain stimulation,

“The dream here ought to be integration by training and by educational and scientific interests to bring people together in a model that has never been done before.” — **Dr. Joseph B. Martin, Co-Founder and Co-Chair of the Harvard NeuroDiscovery Center, Harvard University, and former Dean of the Faculty of Medicine, Harvard Medical School**

neurophysiology and neuropsychology, stroke, neurogenetics, developmental neuroscience, stem cell biology, medical devices, and degenerative diseases of the brain, including Alzheimer’s and Parkinson’s diseases.

Yet in the face of the accelerating pace of brain research worldwide, mere continuation of Ontario’s efforts status quo will cause the province to fall behind. To carve out a leadership position, and to benefit fully from the wise investments in neuroscience that Ontario has already made, we need to move beyond the traditional model of funding “curiosity-driven” research — often carried out independently or by small groups of like-minded colleagues. While this type of research is essential and must continue, Ontario can increase its effectiveness by approaching brain research through a new, collaborative model that brings experts together across disciplines and institutions, breaking down silos, building upon the province’s existing strengths and ensuring ever-greater gains in knowledge and clinical applications. Such a model will differentiate Ontario from the pack of other countries and jurisdictions.

In this proposal we recommend the establishment of a province-wide brain research institute — tentatively titled the Ontario Brain Institute (OBI) — that will bring together Ontario’s best clinical and basic neuroscientists along with newly recruited professionals in pursuit of common research problems.



This group of professionals will work collaboratively on defined projects of common interest aimed at creating new knowledge about the brain and on translating that knowledge to the care and treatment of patients suffering from diseases of the nervous system. **In short, the key to Ontario’s success within today’s worldwide brain research revolution will be a well-designed, well-led program focused on bringing together for the first time Ontario’s most skilled clinical and basic neuroscientists in a common effort.** As described later, the Institute will be organized in a hub and spoke fashion, with a central unit housing platform technologies interacting with teams of scientists and clinicians drawn from Ontario’s universities, colleges, and hospitals.

Advances in brain research are dependent on this type of collaborative effort, for a true understanding of the brain will arise not from one discipline alone, but from the working together of experts from multiple disciplines including clinical investigators, basic scientists, engineers, computer specialists, molecular biologists, geneticists, mathematicians, and others. Ontario is an ideal setting for such a collaborative approach, in that the province’s academic medical research community is large enough to be multi-talented but small enough to be interactive; the quality of research here is as good as anywhere in the world; and Ontario scientists pride themselves on collegiality, on being supportive of one other, and on being dedicated to understanding human diseases. Along with scientific advances, this relatively new culture of scientific collegiality is part of the reason that the timing is right for a transformational effort in Ontario.

Furthermore, bringing together clinical and basic neuroscientists and dissolving the boundaries that separate disciplines should be of enormous value in creating intellectual property for commercialization. Currently, Ontario’s commercial neuroscience industry is not as robust as its international competitors and some of its Canadian competitors; and yet the potential is huge. Diseases and disorders of the brain afflict more than 2 billion people worldwide, with an annual economic impact of \$2 trillion.² In 2007, neuropharmaceuticals generated \$109 billion in revenue, neurodevices generated \$5.5 billion, and neurodiagnostics generated \$16 billion. The biotech giant Genentech, for one, has embarked upon a major commitment to brain research, for, as the company’s executive vice president for research and early development, Dr. Richard Scheller, explains:

“We’ve learned enough about neuroscience — from finishing the genome, to all we’ve learned about ion channels and signal transduction and development — to think more rationally about diseases. It’s not going to be easy, but in our opinion, it’s time to get really, really serious about neuroscience.”³

A SPOTLIGHT ON CURRENT COLLABORATION

Recently, as a result of this initiative, a research project has been established that will serve as a prototype for collaborative research and training in neuroscience. The research goal is to understand the neural mechanisms through which deep brain stimulation (DBS) induces changes in brain activity including reducing tremors in Parkinson’s disease patients and elevating mood in patients with treatment-resistant depression.

The research team includes neurosurgical investigators from the Toronto Western Hospital, computational neuroscientists from the Rotman Research Institute at Baycrest, and neurophysiologists from the Robarts Institute at the University of Western Ontario. \$4 million has been contributed towards the costs of brain imaging and computational modelling, with matching funds of \$6 million provided by the participating organizations. Additional funding of \$1.4 million will be provided to support a postdoctoral training program to support the initiative.



**GLOBAL REVENUE GENERATED IN 2007
FROM NEUROPHARMACEUTICALS,
NEURODEVICES, AND NEURODIAGNOSTICS
EXCEEDED**

**\$130
BILLION**

**"... IT'S TIME TO GET
REALLY, REALLY SERIOUS
ABOUT NEUROSCIENCE."**

— Dr. Richard Scheller, Executive Vice-President, Genentech

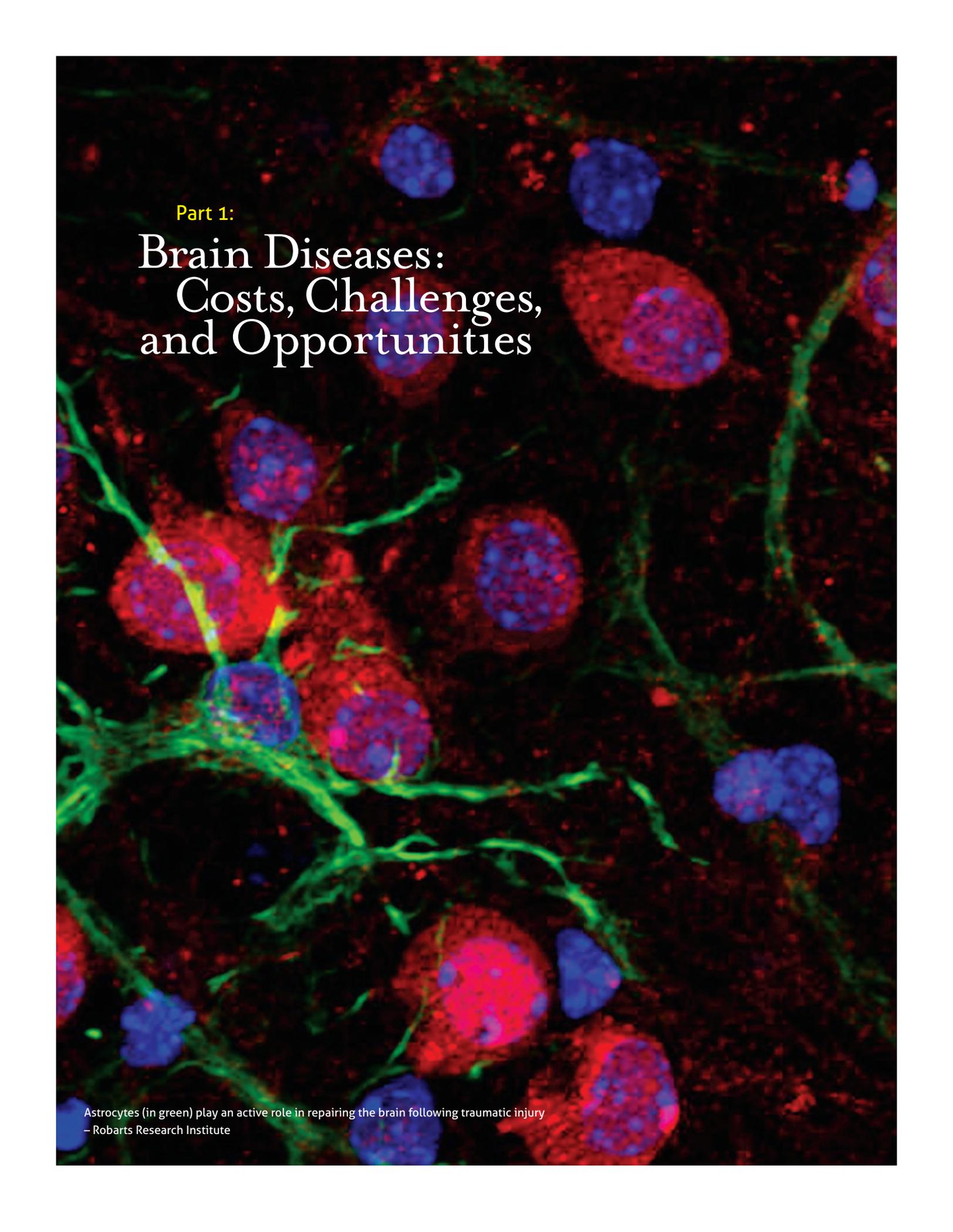
Therefore, in addition to meeting the clinical challenges that face the province and the other benefits that are outlined, one of the main reasons that Ontario should support this initiative is to promote the development of neuroscience intellectual property, which will have downstream effects in supporting Ontario's efforts to promote its knowledge-based economy.

The impact of the OBI will be significant for the province:

- Ontario will be recognized internationally as a leading jurisdiction in translational brain research, attracting top talent in basic and clinical neuroscience. The province will also become a unique training ground for the next generation of scientific and clinical leaders in interdisciplinary brain research and treatment.
- Ontario will become a leader in the translation of brain-research-generated innovations from the laboratory to the clinic, which will improve medical care in the province and reduce the economic and social burdens associated with brain diseases. Discoveries will lead to innovative treatments for brain diseases, accelerated access to novel therapies, and improvements in the quality and efficiency of health care delivery.
- Ontario will be well positioned to capitalize on the commercial potential for neuroscience research, attract new investment, create spin-off companies, and generate high-value jobs in technologies associated with brain research and clinical care. Neuroscience research will become a driver of commercial activity that can help to fuel the competitive growth of Ontario's knowledge-based economy.



Preparing a patient for deep brain stimulation – Toronto Western Research Institute

A fluorescence microscopy image showing brain cells. The nuclei are stained blue, and the cytoplasm and some organelles are stained red. A network of green filaments, representing astrocytes, is visible throughout the field of view. The background is dark, making the colored structures stand out.

Part 1:
Brain Diseases:
Costs, Challenges,
and Opportunities

Astrocytes (in green) play an active role in repairing the brain following traumatic injury
– Roberts Research Institute



**38% OF YEARS LOST TO DEATH AND
DISABILITY ARE DUE TO BRAIN DISORDERS.
— WORLD HEALTH ORGANIZATION**

SOCIETAL IMPACTS OF BRAIN DISEASE

The prevalence of brain diseases and disorders in Canada and other western societies is staggering in its magnitude, with huge deleterious effects on society. Clinical depression... autism... bipolar disorder... Parkinson's disease... Alzheimer's disease — an estimated 1 in 4 Canadians (8.25 million) will suffer from these or other brain diseases in their lifetime.

Perhaps one of the most important societal impacts of brain diseases is one that eludes measurement: Canada's future ability to compete internationally in a knowledge-based economy will depend upon the creativity, knowledge, and skills of our people; mental disorders and neurological diseases erode this collective capacity.

Globally, the World Health Organization attributes 38% of the total years lost to death and disability to brain disorders, a figure well ahead of the next-closest and higher-profile diseases of cancer (12.7%) and cardiovascular disease (11.8%).⁴ These numbers reflect a reality that is already tragic for individuals and families and is potentially catastrophic for the health system, social systems in general, and for our economic prosperity.

Moreover, the rates of disease incidence are increasing, especially among children and young adults. As one example, 10 years ago the accepted incidence rate of autism spectrum disorders (ASD) in Canada was about 1 in 2,000, but is now estimated by the Geneva Centre for Autism as being 1 in 165 individuals. In the United States in 1992, some 16,000 children were diagnosed with ASD, and by 2007 the number had risen to 260,000 — a 16-fold increase (although it should be noted that awareness of these disorders has also increased, so that many more children are diagnosed today than previously). The same alarming picture holds at the other end of the life course. Within Canada, over 500,000 Canadians (1 in 11 seniors) presently suffer from Alzheimer's disease or a related dementia.⁵ By 2011, the annual increase is forecast to be over 100,000 new cases per year;⁶ and if nothing changes within 25 years, the number of Canadians with Alzheimer's disease or a related dementia will be one million. The prevalence of the disease doubles every 5 years after age 65, and Statistics Canada forecasts that the number of Canadians 65 years and older will more than double from 2006 to 2031, amounting to a total of 9.1 million people, or 23.4% of the Canadian population.⁷

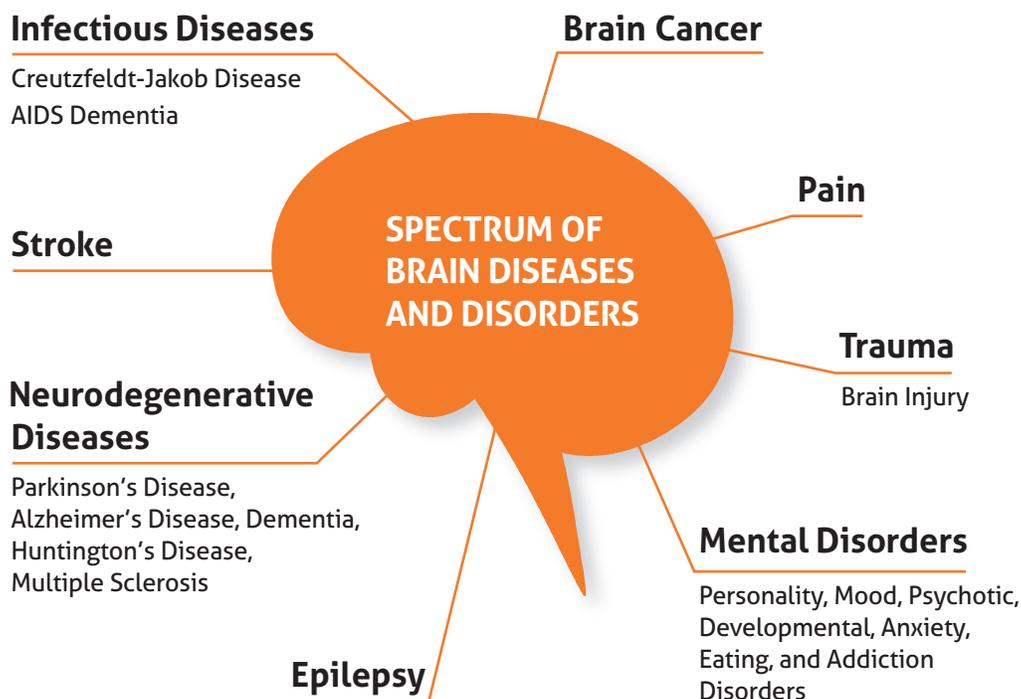
Other illnesses that affect mental functioning and thus impair productivity and life satisfaction include Parkinson's disease, which affects approximately 1.5%–2.0% of people over 60, and bipolar disorder, which occurs in about 2% of the adult population and typically begins in adolescence and early adulthood.

These brain-related diseases and disorders are generally chronic in nature and currently incurable. Many are disabling for long periods of time — in some cases throughout life — resulting in long-term care, reduced productivity, and costly disability assistance programs for lengthy periods. Medication is often directed at alleviating the symptoms without addressing the underlying mechanisms. Furthermore, the burden on society of brain diseases increases yearly as the population ages and as the baby-boomer generation reaches age 65 and beyond.

The impact of brain diseases on patients and their families is distressingly clear. Less obvious is the burden on caregivers, who may have to curtail work hours or even give up work entirely, with corresponding losses to personal income and provincial productivity. Almost 4% of Canadians are now caring for a family member, with 39% of these cases (350,000) entailing Alzheimer’s disease or a related dementia.⁸

The impact of brain diseases and disorders on Ontario’s economy is significant, with the cumulative financial burden estimated to be \$39 billion,¹ broken down as follows: public expenditures (direct health costs and other direct costs) at approximately \$7.5 billion annually⁹ and lost workplace productivity attributed to short- and long-term disability or death at \$28 billion annually.¹⁰ Included in this figure is the cost to business for disability insurance claims and workers’ compensation claims, which the Ministry of Health and Long-Term Care estimates to be in excess of \$2 billion. And these figures do not even include dementia-related disorders.

The societal impacts of brain diseases are wide ranging and go far beyond the dollars spent within Canada’s health care system or calculated in lost work productivity. Brain disorders in children dramatically affect the education system, which is charged with responding to students’ special learning needs. And the incidence of such needs is large: Statistics Canada data for 2001 indicate that over 182,000 children in Canada (3.25% of children aged 0 to 14 years) have various brain-related disabilities.¹¹ A total of 12.5% of Ontario students now receive special education programs, at a cost of \$2.1 billion, and approximately half this burden derives from neurologically related issues.¹²



Adults unable to participate fully in society place demands on the country's social safety nets — its social assistance, welfare, and disability programs. Over half of the 348,515 beneficiaries of Ontario's Disability Support Program (\$3.3 billion in 2008–2009) have neurologically related issues.¹³ The cost for this support is almost as large as the cost of the entire welfare program in Ontario (Ontario Works). Given the strong links among homelessness, addictions, crime, and mental disorders, Ontario's policing, courts, and corrections programs and facilities are affected as well.

The pressing imperative to address the treatment and prevention of brain-related diseases has ignited a revolution in how we approach diseases scientifically. To date, medical science has been able to treat some of the symptoms of neurological diseases and disorders but has not found cures — yet there is now more reason for optimism than ever before: A cascade of recent advances in medical research and technology has brought neuroscience research to the cusp of a deeper understanding of brain physiology that, in turn, will lead to disease-modifying therapies for neurological diseases and disorders.

Indeed, this optimism has fuelled a huge, worldwide surge in investments in brain research on the part of governments and the private sector. The potential market opportunities capturing the attention of the private sector are set out in the next section.



Courtesy of Baycrest Centre for Geriatric Care

COMMERCIAL POTENTIAL OF BRAIN DISEASE RESEARCH

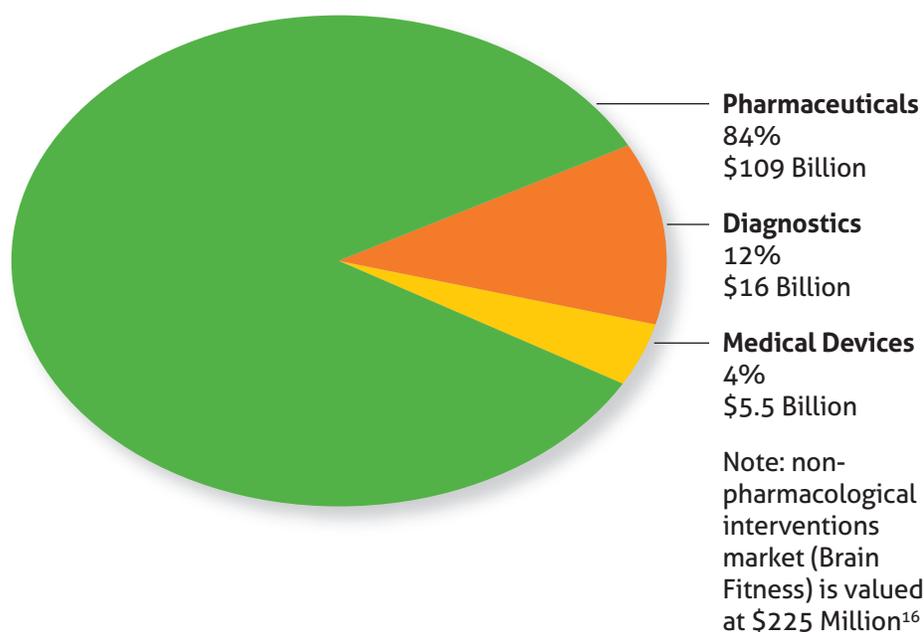
In addition to the medical and societal benefits, advances in neuroscience research will lead to the development of products and commercial applications such as diagnostics, devices, and therapies with significant market value. Large multinationals including pharmaceuticals recognize the size and growth of the market in brain-related products and are making large investments into this area.

A large and growing — but challenging — market for central nervous system health products

The growing prevalence of brain diseases, plus the recent cascade of promising scientific advances, has prompted renewed interest on the part of industry in developing and commercializing brain health innovations. The 2007 global market for central nervous system (CNS) diagnostics and therapeutics was valued at \$130.5 billion, second only to the market for cardiovascular therapies (*Figure 1*).^{14,15} Going forward, driven by the demand for more effective pharmaceuticals, medical devices, diagnostics, and non-pharmacological interventions, the CNS market is projected to grow by 10% per year, reaching over \$300 billion by 2018.

Figure 1

CNS MARKET SIZE AND GLOBAL SALES BY SECTOR



Despite the new knowledge and significant advances created in research laboratories over the past decade, significant limitations remain in our knowledge about brain diseases — gaps that continue to hinder the translation of brain research discoveries to commercialized products aimed at preventing, diagnosing, and treating brain diseases.

Market potential and commercial challenges within the four market sectors of pharmaceuticals, medical devices, diagnostics, and non-pharmacological interventions are discussed in the following section.

1. PHARMACEUTICALS

Market potential

Global pharmaceutical sales reached \$109 billion in 2007, with an annual growth rate of 6.4% (2006–2007); in the United States, the value of CNS pharmaceutical sales currently exceeds that of both cancer and cardiovascular disease. Because the mechanisms underlying brain disease remain largely unknown, most available pharmaceuticals provide only symptomatic relief and are often used non-specifically across disorders. Thus, there is tremendous medical need as well as corresponding market potential for disease-modifying therapies.

Given the aging population and the inability of current interventions to alter the course of brain pathologies, the sector will see continued growth across the three major CNS disease areas:

- i. **Psychiatry.** Anti-psychotic, anti-depressant, and anti-convulsant drugs currently dominate the CNS market and include several blockbusters that are useful for treating several CNS disorders.
- ii. **Neurology.** Although only half the size of the psychiatry market, therapies for neurological diseases (such as Alzheimer’s disease, Parkinson’s disease, multiple sclerosis, and epilepsy) show the highest growth rate (a combined annual growth rate for 2004–2007 exceeding 11%). This trend is set to continue, propelled by increases in the aging demographic.
- iii. **Pain.** Though the market is highly saturated with both branded and generic drugs to relieve pain, current pain-management options continue to be inadequate for the large number of patients suffering acute and chronic pain. This will continue to stimulate new R&D investment.



Commercialization challenges

Unlike cardiovascular disease and cancer, for which validated drug targets have permitted the development of disease-modifying therapies, most CNS therapies target disease symptoms only. Major challenges hindering CNS drug development include:

- A lack of understanding about what causes neurodegenerative diseases and developmental disorders of the brain, including mental disorders, thus hindering the creation of useful animal models for their study.
- A lack of diagnostic markers to predict disease onset, which has minimized the opportunity to develop targeted therapies suitable for early intervention.
- The difficulty of delivering drugs across the blood-brain barrier to reach intended targets.
- The lack of quantitative end points to assess efficacy in clinical trials.

2. MEDICAL DEVICES

Market potential

Important advances have been made in the CNS medical device sector, including electroconvulsive therapy (ECT) used in treating depression, and DBS in treating Parkinson's disease. A concerted effort is now under way to develop assistive devices that enable aging seniors to continue living independently. These include devices to assist individuals with cognitive, sensory, and physical challenges, along with their caregivers, and “intelligent environments” that facilitate activities of daily living and monitor changes in health.

Commercialization of device technologies differs from drug development in several important ways. First, assistive devices can be developed and approved for use quickly and inexpensively while drug development generally requires years of basic science research, followed by staged clinical trials, which require years of investments and often prove to be unsuccessful.

Commercialization challenges

The therapeutic CNS medical device sector is nascent and currently grappling with concerns over intellectual property and long-term safety. Key challenges in the area include:

- The lack of predictive animal models, which has forced companies to invest disproportionately in costly, high-risk development work in the clinical setting.
- Concerns over the long-term safety of surgically implanted devices.
- Growing requirements for longer and more complex clinical trials, resulting in high development costs and prohibitive return on investment.
- The ability to secure US patent protection for the development of deep brain stimulation techniques targeting entire regions of the brain, restricting innovation in this promising area.

“The entire field of neuroscience now has the tools to make phenomenal advances. Ontario can lead a revolution in neuroscience, the goal being the healthy brain.” — **Dr. Bryce Weir**, Goldblatt Professor Emeritus of Surgery and Neurology, former Director of the Brain Research Institute, Interim Dean of the Biological Sciences and Pritzker School of Medicine and Vice-President for Medical Affairs, all at The University of Chicago

3. DIAGNOSTICS

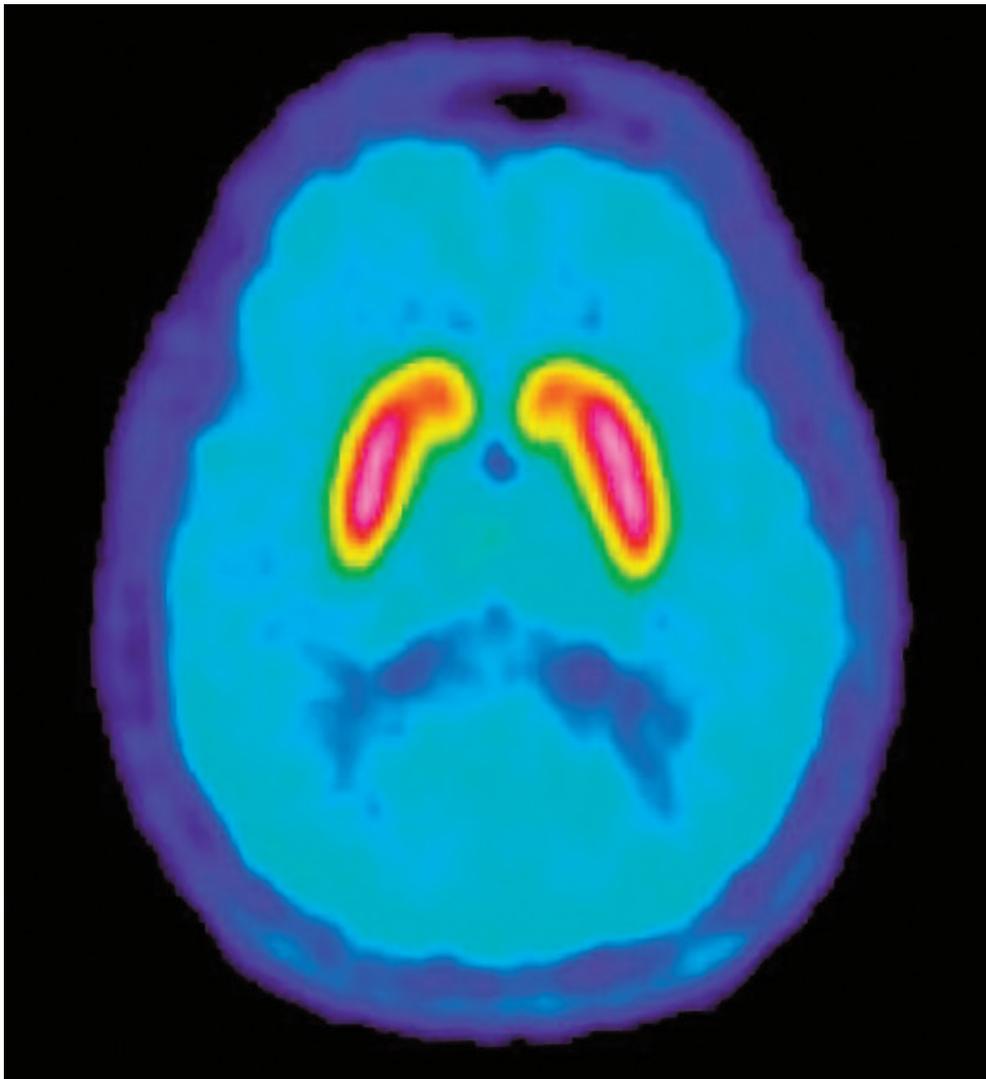
Market potential

The CNS diagnostics sector has long been dominated by large advanced-imaging devices such as magnetic resonance imaging (MRI), electroencephalography (EEG), and positron emission tomography (PET). The future of the diagnostics market lies in CNS biomarker discovery, an area of intense industry priority that is second only to cancer biomarkers.

Commercialization challenges

Poor understanding of brain disease mechanisms has impeded the discovery of predictive biomarkers for diagnosis and staging and, by extension, the full exploitation of imaging technologies. Key challenges include:

- The absence of disease-modifying therapies, which has limited the usefulness and value of diagnostics capable of early detection of disease.
- The costs of current imaging equipment, which is expensive to own, operate, and maintain.

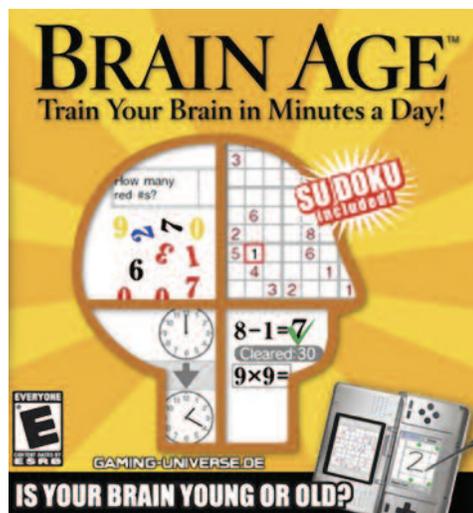


PET image of dopamine availability in deep brain structures – Centre for Addiction and Mental Health

4. NON-PHARMACOLOGICAL INTERVENTIONS

Market potential

This catchall market sector includes an array of preventative, assessment, and therapeutic products aimed at maintaining brain health. The US brain fitness software market, estimated at \$225 million in 2007, is growing rapidly and driven primarily by products targeting the consumer market, although currently there is no empirical evidence, to our knowledge, that these products being marketed to improve brain health are effective. The development of evidence-based, clinically validated technologies for improving brain health holds great potential for impacting the development of strategies for treating or preventing CNS diseases. Increased understanding of brain functioning has the potential to lead to unanticipated applications with respect to marketing, advertising, technology tools for learning, and technology assistance for complex jobs (e.g., aerospace simulators).



Commercialization challenges

The lack of clinical validation of the efficacy or long-term benefit of non-pharmaceutical interventions such as “brain fitness” products has limited their adoption as part of a standard disease prevention/treatment regimen.

Ontario’s neuroscience industry

Ontario’s brain research community has generated some noteworthy commercial successes, including the creation of spin-off companies and the licensing of promising technologies to industry receptors (*see table on next page*). However, much more can be done to exploit the wealth of basic science research discoveries being made in the province. Towards that end, the province needs to improve its record in patenting intellectual property, in creating spin-off companies, and in transferring technology to industry receptors.

With a base of 18 small and medium-sized enterprises (SMEs) and one multinational enterprise (MNE) actively conducting discovery-stage brain research, Ontario compares favourably with other jurisdictions of similar size in sheer number of firms. But the majority of Ontario’s SMEs are small, early-stage, and isolated, as well as inadequately supported by the larger, innovation-driven firms that foster and sustain mature clusters. This problem is consistent with the challenge of commercialization in other Ontario sectors, which has been identified for improvement in a number of reviews.¹⁷ By way of illustration, a comparison of Ontario’s neuroscience landscape with three emerging or established US clusters (North Carolina’s Research Triangle, San Diego, and San Francisco) shows Ontario’s industry as lagging in technology transfer, commercial success, venture capital funding, and industry investment per capita.

ONTARIO BRAIN RESEARCH COMMERCIAL ACHIEVEMENTS

DIAGNOSTICS

Gene-based diagnostics for early-onset Alzheimer's disease (licensed to Athena Diagnostics)

Gene-based diagnostics for macular degeneration (Arcticdx)

Gene-based test for Tardive Dyskinesia (licensed to Clinical Data Inc/ PGxHealth)

Gene-based test for antidepressant-induced mania (licensed to Pfizer Corp)

Gene-based test for Rett's Syndrome (licensed to Athena Diagnostics)

Antibody diagnostics licensed to: Affinity Bioreagents, Athena, Covance Research Products, Isis Innovations, Schering-Plough

THERAPEUTICS

Small molecule inhibitors of A β aggregation (spin-off companies: Neurochem and Ellipsis NeuroTherapeutics / Transition Therapeutics)

Novel therapeutic targets (licensed to Isis Innovations, Schering-Plough)

Deep brain stimulation paradigms for advanced Parkinson's disease and depression (spin-off company: Functional Neuroscience)

Modulators of neuronal apoptosis in Huntington Disease (licensed to AeGera, Neurologix)

Consultations with local and global industry leaders have yielded the following insights into Ontario's performance in the translation and commercialization of new knowledge created by brain research:

Ontario's commercial assets include:

- Globally recognized expertise in basic brain research, discussed below in detail.
- Established expertise and access to all aspects of clinical neurology, neurosurgery, and psychiatry.
- Access to clinical trials.
- Access to large patient populations.
- Availability of primate facilities for preclinical studies.
- Existence of nascent industry base and angel investors capable of seeding cluster growth.

Ontario's shortcomings include:

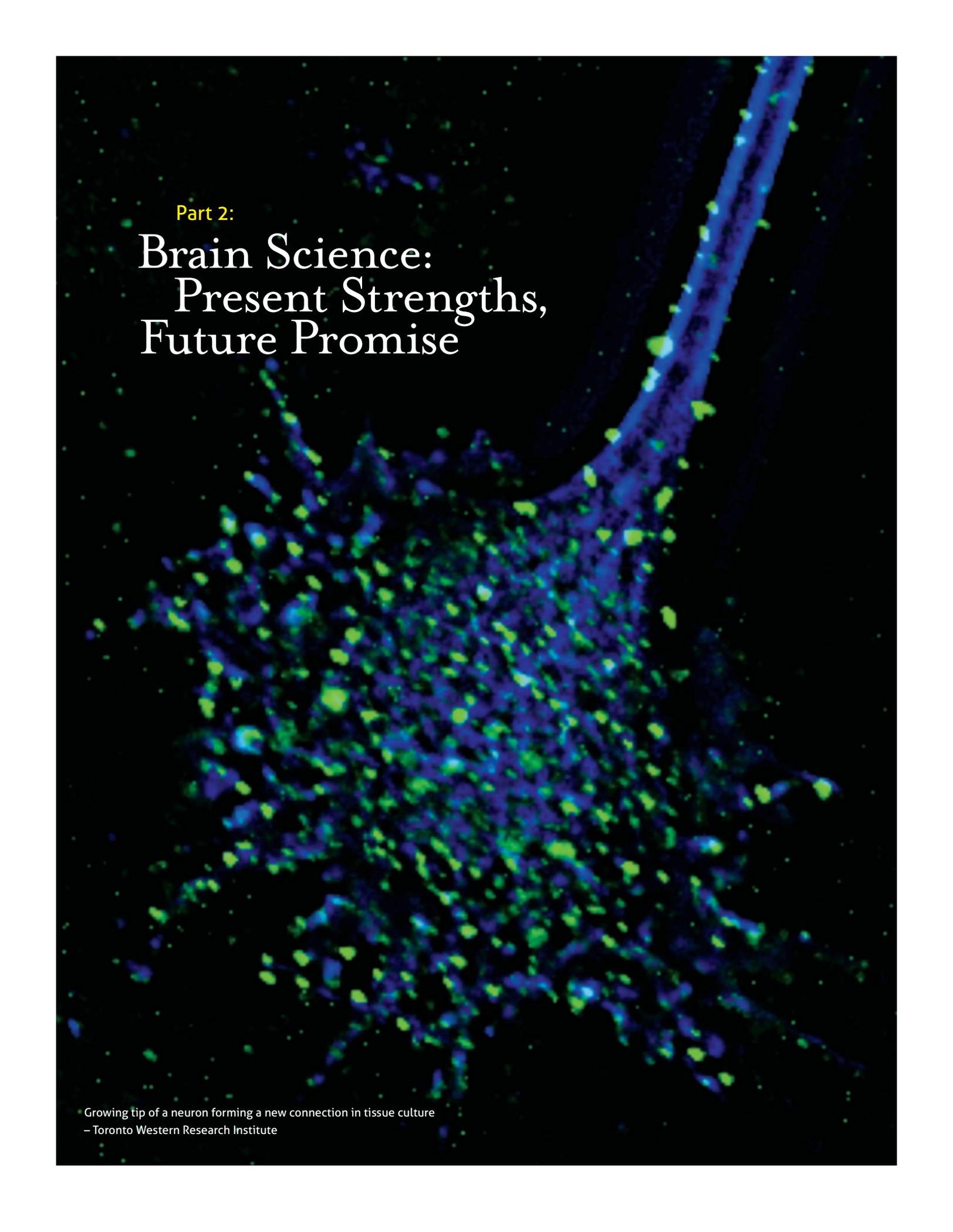
- Patenting activity that is minimal and less than that of its peers.
- A lack of multinational enterprises interested in CNS diseases that conduct basic brain research in the province.

Fuelling the growth of Ontario’s neuroscience cluster

Notwithstanding these challenges, Ontario’s globally competitive scientific environment already provides the strong foundation necessary for a successful, innovation-driven CNS industry. Industry leaders have enumerated the following core opportunities to enhance the transfer and development of technology, and so spur industry growth in Ontario.

INVESTMENT AREA	OPPORTUNITY
BASIC AND APPLIED RESEARCH	<ul style="list-style-type: none"> • Multidisciplinary research to elucidate basic disease mechanisms and to identify targets, biomarkers, and the rationale for treatment design. • Development of animal models more representative of pathological disease states and more predictive of treatment efficacy. • Early-stage research to catalyze the development of diagnostics and treatments for rare CNS disorders. • Research in pioneering areas with the potential for high impact on the CNS field (e.g., stem cells).
CLINICAL/ TRANSLATIONAL RESEARCH	<ul style="list-style-type: none"> • Clinical trials to validate existing candidate CNS biomarkers that are currently stalled in Phases I and II due to lack of funding, and to identify quantitative clinical end points relevant to both animal and human trials. • Development of a centre of excellence for CNS clinical trial design that brings together skilled clinician-scientists and statisticians to champion the design of appropriate and adaptive CNS trials, analyze outcomes on a per-patient basis, and translate the knowledge globally. • Construction of a regional framework to mobilize and coordinate translational research and undertake complex clinical trials across Ontario, with support for the dedicated research infrastructure that enables these trials.
CROSS-CUTTING INVESTMENTS TO SUPPORT RESEARCH AND COMMERCIALIZATION EXCELLENCE	<ul style="list-style-type: none"> • Forums aimed at increasing dialogue and research collaborations to showcase and support the growth of Ontario’s nascent CNS cluster. • Creation of research platforms to support CNS R&D across disorders (e.g., tissue repositories, integrated databases, high-throughput screening).

Thus, industry leaders agree that today’s revolution in neuroscience research offers opportunities not only for improved patient care but also for products of great commercial value. In the following section, we look more closely at the research advancements that have led to this optimism and evaluate Ontario’s strengths relative to other international jurisdictions.

A fluorescence microscopy image showing a neuron tip forming a new connection in tissue culture. The neuron is stained with blue and green dyes, and the background is dark with scattered green spots. The neuron's tip is visible on the right side of the image, extending towards the center.

Part 2:

Brain Science: Present Strengths, Future Promise

Growing tip of a neuron forming a new connection in tissue culture
– Toronto Western Research Institute



The human genome is stored on paired chromosomes as illustrated

RECENT ADVANCES IN NEUROSCIENCE

Most neurological diseases of the brain, spinal cord, and peripheral nervous system, along with psychiatric disorders, are currently incurable, and their causes are still not understood. Yet the expectations today are stronger than ever before that breakthroughs in our understanding of brain function will lead to disease prevention, effective treatments, and cures.

What fuels this growing optimism?

It is based on the development of new technologies that have allowed us to study all levels of brain function. Because of these technologies, major advances in our understanding of the brain are occurring at an unprecedented rate at the genetic, cellular, circuit, and behavioural levels, across all developmental stages of life from birth to old age, in health and in illness. Risk factors for disease, both inherited and environmental, are being identified, and biomarkers of disease are being developed. In short, we are making rapid and significant progress in unravelling the most complex structure in the universe — the human brain.

Technological advances that have generated this revolution in brain research include the following.

Genetics. The sequencing of the human genome has elucidated every gene in every cell of the body. In the brain, the challenge of understanding gene function would seem to be overwhelming, since the brain contains 100 billion nerve cells located in separate brain regions with different functions. Yet major progress towards mapping gene distribution within the brain has been achieved, and neuroscientists are determining the functions of these genes by using experimentally manipulated mouse models, amplifying the genes' activities or removing them entirely through gene-knockout technology.

As well, experimental methods now make it possible to turn genes on and off at will in specific populations of brain cells in young and adult mice. These studies are allowing us to better understand how gene abnormalities give rise to such diseases as Huntington's disease, amyotrophic lateral sclerosis (ALS), spinocerebellar ataxias, and fragile-X syndrome.

Stem cell biology. For the first time, neuroscientists have access to human embryonic stem cells, from which all tissues of the body arise. These cells have tremendous potential to help us understand brain function, for they provide an opportunity to study the cell biology of the developing human brain. Major advances have already been made. For example, genes that direct the differentiation of nerve cells into different functional subtypes have been identified, as have other genes that promote nerve cell growth and keep developing nerve cells alive.

Understanding brain development is central to our understanding of brain diseases, given that many of the genes and proteins that regulate early brain development function throughout life to maintain a healthy brain. Furthermore, mental diseases that appear during early childhood, such as autism, and in the teenage years, such as schizophrenia, are probably due to abnormalities in brain development. Clearly, a first step in understanding these diseases is to understand the principles that regulate brain development.

Brain circuits. Brain mapping requires understanding not only how genes and cells are distributed in the brain, but also how brain cells interconnect in circuits to carry out brain functions. Circuit analysis in complex organisms is now possible as a result of recently developed innovative tools. These include:

- Viruses genetically engineered to traverse synapses-connecting neurons. These viruses can be engineered to emit colours, which allow the infected neurons to be identified and traced under the microscope. In this manner, scientists can determine their routes within brain tissues and track their connections.
- The brainbow technique, in which fluorescence-coding genes producing red, blue, and yellow colours are genetically introduced into nerve cells in differing amounts, resulting in hundreds of different colours. This technique has allowed scientists to differentially label neurons within a single nerve cell population and to plot their courses and relationships.
- Light-switch technology, through which scientists can introduce into nerve cells a gene coding for a protein called channel rhodopsin-2. When exposed to blue light, this protein incites nerve cell activity by allowing the flow of sodium ions across the membrane and into the cell. In the absence of light, the protein becomes inactive, ion flow ceases, and the cell shuts down. This technology is now being used to map the functions of specific populations of nerve cells within the brains of experimental animals.

Addictions. Recent research has shown that drug addiction is a complex but treatable brain disease. One line of research has tied drug dependence to the same brain structures that regulate learning and memory; drugs that disrupt learned associative bonds may therefore be useful for treating addictions. Other studies have shown similarities between patients with damage to areas of the prefrontal cortex and individuals with addictions; both choose immediate rewards and ignore risks of future negative consequences. In short, neuroscientists are now beginning to understand which brain regions and circuits are involved in addiction; this has huge potential to create new therapies and to alleviate one of society’s most troubling — and most costly — problems.

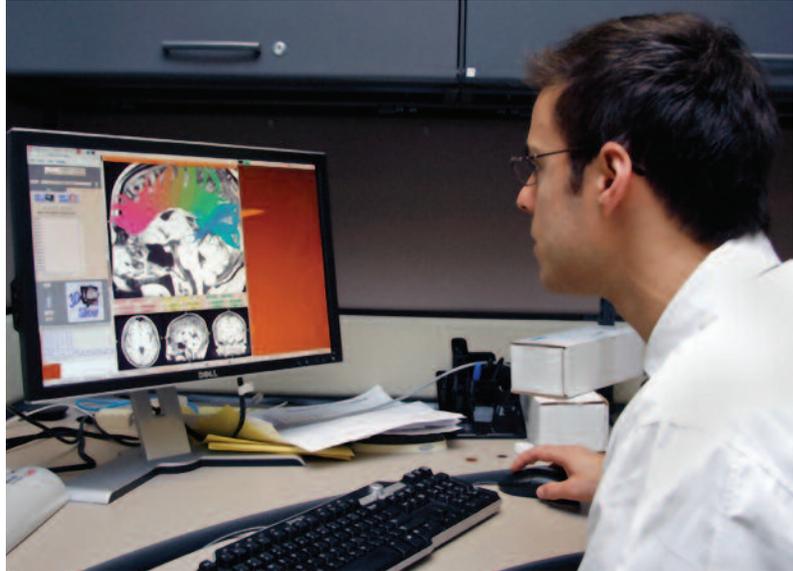
Brain plasticity. Neuroscientists increasingly recognize that experiences and environmental influences can alter brain structure and function across the entire lifespan, not only during early development but also in adulthood and old age. These external influences induce brain changes, probably as a result of altering the expression of genes rather than by changing their structure. Such “epigenetic” changes can arise as a function of changes in the animal or human’s external environment. This increased understanding of how our genetic inheritance interacts with environmental changes is providing crucial insights into the growth and maintenance of brain structure and function.

“A revolution has taken place... is taking place.
Ontario should take advantage of it.
There are things you couldn’t do five years ago.”

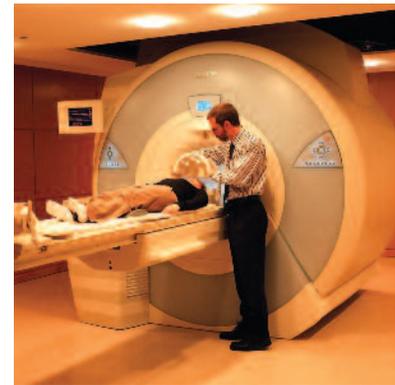
— Dr. Martin Raff, Emeritus Professor of Biology, Medical Research Council
Laboratory for Molecular Cell Biology at University College London

RIGHT: Studying computerized images from a brain scan – Centre for Addiction and Mental Health

BELOW: Preparing a patient for functional MRI scanning – Baycrest Centre for Geriatric Care



Brain imaging. New methods of brain imaging have allowed scientists to investigate both the structure of the brain and how its dynamic activity relates to our ability to perceive, pay attention, remember, think, and make decisions. MRI and computed axial tomography (CT) provide high-resolution images of brain structures and have been of major assistance in diagnosing tumours and brain diseases. Brain activity is also being measured by PET and fMRI, both of which measure the dynamics of blood flow within the brain. Researchers also use various techniques to measure the brain's electro-magnetic activity; these include EEG, magnetoencephalography (MEG) and transcranial magnetic stimulation (TMS). Taken together, these techniques allow us to monitor brain activity safely and non-invasively in living humans — a major step forward in understanding brain function.



Deep brain stimulation (DBS). The technology of electrically stimulating deep brain centres has helped alleviate the symptoms of more than 55,000 patients suffering from Parkinson's disease, essential tremor, treatment-resistant depression, and obsessive-compulsive disorder. As yet, we do not understand how DBS works, but clearly its effectiveness raises prospects for its use as a significant treatment modality in otherwise untreatable neurological diseases. In addition, DBS promises to become a useful tool for understanding the circuitry of the brain and the role of specific nerve tracts in neurological and mental disorders.

Computational neuroscience. The human brain is far too complex to understand intuitively, and for that reason the new and rapidly emerging science of computational neuroscience is becoming an essential tool in all aspects of brain research. This interdisciplinary science has enormous power, not only to integrate and interpret data across traditional boundaries, but also to create new theories of brain function to be tested experimentally.



**CANADA?
ONTARIO?**

Cognitive neuroscience and neuropsychology. Cognitive neuroscience — the study of attention, perception, memory, learning, and thinking — has literally undergone a revolution in the last 15 years with the advent of such functional neuroimaging technologies as fMRI, PET, and MEG. It is now possible, for example, to observe the neural mechanisms of attention and perception, and also how memories are encoded and subsequently retrieved.

The term neuropsychology refers to the study of brain organization through observations and tests of clinical patients. Researchers in this area record areas of brain damage and relate them to observed deficits in perceptual, motor, and cognitive behaviour. In this way, individual cases can provide evidence for the nature and brain locations of different cognitive functions.

GLOBAL INVESTMENTS IN BRAIN RESEARCH

Governments worldwide suffer the burdens of chronic incurable brain diseases through increased health care costs, lost productivity, and massive pressures on social safety nets. Recognizing that neuroscience research is at the beginning of a revolution with the potential to significantly improve the prognosis of these patients, many jurisdictions are making major investments in brain research to ensure that they both contribute to and benefit from this revolution, with benefits to the people they serve. Indeed, *Frontiers in Neuroscience* commented on

“...the rapid blossoming of new brain research centers in many locations worldwide with massive investment of billions of dollars in many countries from both private foundations and government sources.”

Major investors include the United States, China, Australia, Japan, Brazil, United Kingdom, Germany, France, and Portugal (but not Canada). The following is a sampling of new or expanded international brain research programs worthy of note.

University College London (UCL) is a world leader in the genetics of neurodegenerative disease, in cognitive neuroscience, and in cellular and molecular neuroscience. UCL was recently awarded a major grant to establish the Sainsbury-Wellcome Centre for Neural Circuits and Behaviour, which will investigate neural circuit elements (cells, synapses, conductance mechanisms) and the way in which neural circuits mediate perception, learning, and other aspects of behaviour.

The German Government has recently established an “Excellence Initiative” cluster in neuroscience to study neurodegenerative diseases. Headquartered in Bonn, the program will link scientists from Germany’s leading research centres to work together on developing therapies for neurodegenerative diseases. As well, a German family has awarded a philanthropic grant of 400 million euros (\$620 million CAD) to the Max Planck Institute in Frankfurt to establish a new institute in cognitive brain research.

The Chinese Academy of Science founded the Institute of Neurosciences in Shanghai in 1999. It currently has 24 laboratories with a total of 250 research staff, including students and postdoctoral fellows. Research focuses on molecular and cellular mechanisms underlying neural development, circuit function, and plasticity; and on mechanisms supporting perception, learning, and memory. The Institute is projected to expand to 50 laboratories by 2020.

Harvard University has recently established an inter-departmental program called the **Center for Brain Science**, which brings together neuroscientists from around the Harvard community, including from its teaching hospitals. Physicists, mathematicians, physicians, and cellular and molecular neuroscientists are studying multiple aspects of brain science. An additional neuroscience program is the **Harvard NeuroDiscovery Center**, formed to provide funding to Harvard researchers who share an interest in solving neurodegenerative diseases. Funding is awarded to research projects that bring together physicians and scientists from within the Harvard community.

Three other major US institutions illustrate how philanthropic gifts can leverage additional private sector funding to catalyze the development of neuroscience research centres that have an immediate international impact. **The Broad Institute** in Cambridge, Massachusetts was launched in 2004 and is jointly governed by Harvard University and MIT; its goal is to transform medicine with genome-based knowledge. One of the Institute's programs is the **Stanley Center for Psychiatric Research**, whose goal is to develop understanding of the molecular underpinnings of severe mental illnesses (e.g., bipolar disease, major depression and schizophrenia) through work on genetics, chemical biology, and neurobiology.

The Allen Institute for Brain Science is an independent, non-profit medical research organization located in Seattle, Washington launched in 2003 with \$100 million in seed funding gifted by Paul G. Allen, the co-founder of Microsoft. The Institute has 125 scientists in neuroscience and related areas, and its research focuses on the interaction of biology and computing, with a view to understanding neural circuitry and its relations to brain functioning.

The McGovern Institute for Brain Research at MIT in Cambridge, Massachusetts focuses on systems of neuroscience — exploring how neurons function within larger brain systems to mediate complex behaviour in both health and disease. There are currently 15 principal investigators (PIs) who study perception, cognition, and action and how these activities relate to brain structure and function. The Institute was founded in 2000 by a philanthropic donation from Patrick and Lore Harp McGovern. Their donation is expected to total \$350 million over 20 years.

NEUROSCIENCE IN ONTARIO

How does research in Ontario compare to work being done in the United States, the United Kingdom, Germany, Japan, and many other countries? Are we up there with the leaders in the field? Are we in danger of “missing the wave” in this area with so much promise for basic science, clinical applications, and commercial opportunity?

An analysis of neuroscience research in Ontario indicates that the province has a number of world-recognized strengths. Furthermore, benchmarking indices show the province to be a leader in Canada, and Canada to be among the top 3 to 5 countries worldwide in this area of science.

Ontario’s neuroscience strengths

Molecular and cellular biology

Ontario is rich in capable molecular neurobiologists working in cell biology, signal transduction, neural development, the regulation and plasticity of synaptic transmission, neurotransmitter receptor biology and signalling, and RNA biology.

A major focus of Ontario neurobiologists is in characterizing fundamental molecular mechanisms mediating neural transmission. Examples of key discoveries include the identification of factors that control and regulate the release of neurotransmitters — the chemical molecules that allow neurons to communicate with each other.¹⁸

Many Ontario researchers have made transformative discoveries on the fundamental principles of neurotransmitter release and uptake at nerve-cell-connecting synapses in the brain and spinal cord. Key discoveries include mechanisms of regulation and blockade of receptors and their role in the rearrangement and restructuring of synapses (called synaptic plasticity), which underlie the brain’s ability to respond to environmental influences.

Neurodegenerative diseases

The Tanz Institute is a world leader in the genetics and cell biology of neurodegenerative disease, especially Alzheimer’s disease (AD). Research focuses on the molecular mechanisms that cause neurodegeneration in AD and, in particular, the mechanisms by which the presenilin protein complex generates the amyloid- β peptide (A β) that plays a central role in this disease.

This group’s major findings include:

- The discovery of several genes associated with AD, and the discovery that these genes interact within the same metabolic pathway. In turn, this leads to misprocessing of the amyloid precursor protein gene (APP) and the accumulation of a neurotoxic protein A β .
- The development of a robust mouse model of AD that develops amyloid plaques and shows synaptic loss, memory impairment, and accelerated mortality. Numerous academic and industrial researchers are now using this mouse to investigate the mechanisms of nerve cell injury and the effects of potential new therapies.

- The discovery of novel therapies directed at blocking the toxic effects of A β , and thus halting cognitive decline in mouse models of AD; the development of small drug-like inhibitors of A β aggregation and neurotoxicity that are now in human Phase II clinical trials in patients with AD.

Ontario scientists studying Parkinson's disease (PD) and other basal ganglia disorders have the following discoveries to their credit:

- The first description of progressive supra nuclear palsy, and the later identification of the protective role of PINK1 protein to suppress neuronal death and loss-of-function effects induced by specific genetic mutations.
- Using a mouse model of PD, the discovery that mutations in the progranulin gene cause corticobasal degeneration and that a new gene pathway protects nerve cells from dying. In related genetic studies, work has led to the identification of PD-causing mutations in relevant genes, and to characterization of the role of other genes in dopamine neuron degeneration.

Genetics and genomics

Ontario geneticists have made major contributions to understanding the genetic influences that contribute to neurodegenerative diseases and psychiatric diseases.

Some highlights:

- Researchers at Toronto's Centre for Addiction and Mental Health (CAMH) have been leaders in relating gene variants in the receptors for dopamine and serotonin to psychiatric disorders and to treatment response.
- CAMH researchers have led important investigations into unstable DNA mutations in mental illness and are expanding that work to the study of schizophrenia, childhood depression, bipolar disorder, anxiety disorders, eating disorders, addictions, and attention deficit hyperactivity disorder.
- New lines of research include neuroimaging studies of white matter abnormalities and how they relate to diseases such as schizophrenia; work combining genotyping and MRI to explore genetic determinants of stroke recovery; and pharmacogenetic studies — discovering gene variants associated with good and bad responses to specific drugs — an area with great commercial potential.
- The Centre for Applied Genomics at the Hospital for Sick Children is a fast-growing centre producing excellent research on autistic spectrum disorders.

Deep brain stimulation (DBS)

Toronto has one of the largest neurosurgery clinical and teaching groups in North America, and the Department of Neurosurgery at Toronto Western Research Institute is cited by the US National Institutes of Health (NIH) as a world leader in DBS technology, which is being used to treat patients with treatment-resistant depression and Parkinson's disease. This group published the first reports of using DBS for treatment-resistant depression.

“Alzheimer’s disease, Parkinson’s disease, stroke, and vascular dementia collectively clearly represent Ontario’s greatest strength and where the province is already internationally competitive.” — Dr. Samuel Weiss, Director, Hotchkiss Brain Institute, and Professor, University of Calgary Faculty of Medicine

The mechanisms by which DBS alters brain physiology are not fully understood, and much more information is needed about the effects of DBS on neural circuits in order to increase its effectiveness in larger groups of patients and expand its use for other neural diseases. Essential to these efforts will be the increased use of brain imaging, computational neuroscience, and studies of connectivity.

Brain imaging

Brain imaging (also called neuroimaging) is a major strength in Ontario and has been significantly funded by the Canada Foundation for Innovation (CFI) and the Ontario Research Fund, resulting in an unusually high concentration of MRI, PET, MEG, EEG, and some optical techniques in the province. This capital investment, in some ways a response to the province’s strengths in imaging, has also served to bolster the development of imaging research.

Increasingly, discoveries arising from human brain imaging studies are being further explored by imaging in small animals, where the biology can be investigated using cellular, molecular, and genetic techniques. Major centres include the Rotman Research Institute, Sunnybrook, Robarts, CAMH, and, for complementary mouse imaging, a consortium of hospitals and their affiliated research institutes, including Mt. Sinai Hospital, the University Health Network, and the Hospital for Sick Children.

Computational neuroscience

This discipline is an Ontario strength as well as a clear need in contemporary neuroscience research. It is increasingly essential as a means to understanding how both cells and brains compute and to modelling the interfaces between levels of function (e.g., between cells and circuits and between patterns of neural activity and cognitive performance). Institutional strengths are found in the psychology and computer science departments at the Universities of Ottawa, Toronto, Waterloo, and York. Scientists have developed computational models of neural network mechanisms responsible for high-level cognition, including analogy, concept application, theory evaluation, and emotional decision-making. Others have developed algorithms to simulate (and thus understand) learning processes in the visual system.

Learning and memory

Cognitive neuroscience has been an internationally recognized strength of Ontario and of Canada generally for at least 50 years, with theoretical and experimental studies of human memory foremost in the cluster. Strengths include theoretical models, applications to neuropsychological cases, and the neural bases of memory via neuroimaging. The currently dominant model of human memory in terms of episodic, semantic, and other systems was developed at the University of Toronto and the Rotman Research Institute. A further focus has been the understanding of normal age-related declines in memory, with the group at the Rotman Research Institute designated as “best in the world” during a recent site visit.

Brain plasticity

Scientists around the province are working on plasticity, from genes to behaviour and rehabilitation. Efforts are also being made to link plasticity and neural regeneration to stem cell biology. Induced pluripotent stem cells (iPS cells) are being developed to create nerve cell diseases in a dish as well as patient-specific stem cells, with the goal of using such cells as substrates for drug toxicity experiments and therapeutics. The Hospital for Sick Children, Mt. Sinai Hospital, University Health Network, Sunnybrook Health Sciences Centre, Queen’s University, Ottawa Health Research Institute, Lawson Health Research Institute, and the University of Waterloo are major centres for this emerging technology. In addition to making discoveries on molecular mechanisms regulating synaptic transmission, Ontario researchers have made major discoveries on mechanisms of learning and memory, and their dysfunction. Examples of key discoveries include neuronal competition in memory formation, the erasure of fear memories in the amygdala, and the role of the anterior cingulate cortex in fear learning.

Perception and action

Ontario has notable strength in studies of the relations between visual perception and motor action, and investigators have recently formed a consortium of 33 scientists (CAPnet) drawn largely from York University, Queens University, and the University of Western Ontario. CAPnet’s research goal is to understand how the brain uses sensory information to construct an internal perceptual representation of the world that guides purposeful movements, both in health and sickness. Most of the central nervous system — including the cerebral cortex, subcortical brain structures, and the spinal cord — is involved in these processes, so this amounts to understanding how the brain works as a system to guide behaviour.

Stroke

The province has established a strong Ontario Stroke System and Registry of Stroke for the prevention, care, education, and treatment of stroke patients. Because vascular incidents have been associated with many forms of cognitive decline and dementia, the stroke network links stroke with neurodegenerative disease and cognitive and behavioural changes. The Heart and Stroke Foundation has also funded a large cooperative network — The Centre for Stroke Recovery — involving scientists and clinicians from Ottawa and Toronto (Sunnybrook Hospital and Baycrest). One of many important findings is the notion that when a stroke occurs, all affected brain cells do not die immediately, despite the fact they are dysfunctional. This led to the important realization that there is time to interfere therapeutically to return blood flow to the affected region, which in turn led to the successful tissue plasminogen activator (tPA) therapy in acute stroke.

Simple model systems

A number of Ontario researchers are studying the genes responsible for nervous system development, nerve growth and axonal guidance, and cell death using genetically tractable nematodes, drosophila, zebrafish, and mouse models. For these and related studies, excellent centralized transgenic mouse facilities have been developed for use by investigators from multiple organizations. Examples of key discoveries include the identification of numerous genes involved in axon guidance, the identification of novel proteins regulating synapse development, and the identification of genes that regulate neuronal polarity. Information on cell death mechanisms, which are crucial regulators of the nerve cell pruning that occurs in the developing nervous system, may provide a bridge to investigators working in the Ontario Institute for Cancer Research (OICR), since abnormalities in cell death mechanisms are central to the development of a number of cancers.

Medical devices

Ontario's medical device community is extremely active and, because of its critical mass and expertise, is considered Canada's leader in medical device technology. Advances include:

- Strengths in microfabrication, nanotechnology, EEG (64-channel recording), and microfluidics, which could lead to lab-on-a chip analysis and implantable devices.
- Technologies in intelligent systems for supporting the daily living of elderly people, such as monitoring home settings to detect falls, talking systems to prompt or instruct dementia patients through toileting, and eye-tracking technology as a diagnostic for stroke and Parkinson's disease.
- Robotic methods using virtual reality, now in development for testing sensory, motor, and cognitive function. The idea is for robotics to be used for clinical testing to facilitate diagnoses in the young and old.
- Rehabilitation robotics and MRI tools and technologies are presently engaging at least two companies in the province (Sentinelle and Quanser).



Device to test how the brain uses sensory input to control muscle movement – York University

Benchmarking the province's neuroscience research

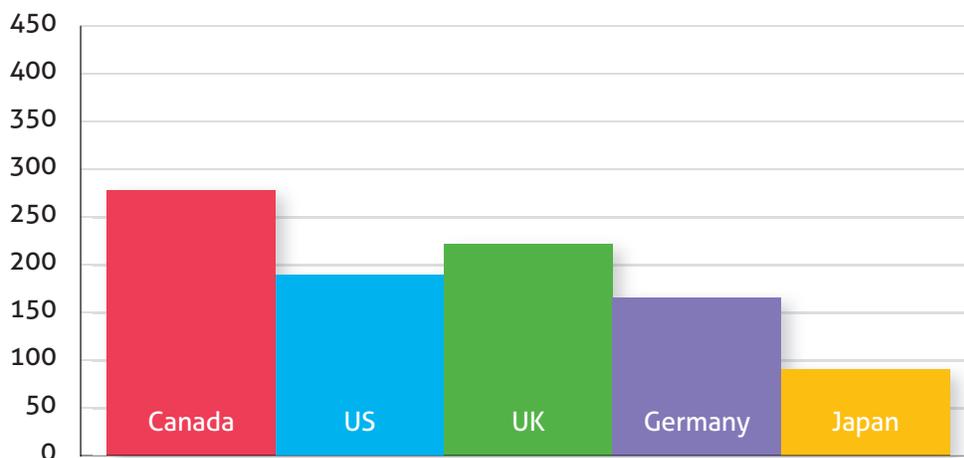
To understand how neuroscience research in Ontario and Canada compares to similar research in other jurisdictions, we carried out an analysis of scientific productivity, research funding, commercialization activity, and distribution of scientists in the neuroscience domain. The specific questions we asked included:

- What is the relative quality and quantity of our activity?
- How do we stack up against other jurisdictions?

We chose to compare Canada to acknowledged international leaders, the United States, the United Kingdom, Germany, and Japan. At a more local level, we compared Ontario to three Canadian provinces, Quebec, Alberta, and British Columbia, and we compared Toronto to Montreal, Canada's two research hubs. We also compared the neuroscience research productivity of Ontario and Toronto to that of the leading states and cities within the United States. Representative data are summarized below.

Figure 1

NUMBER OF PUBLICATIONS 2003–2007 PER MILLION POPULATION BY COUNTRY: NEUROSCIENCE AND BEHAVIOUR



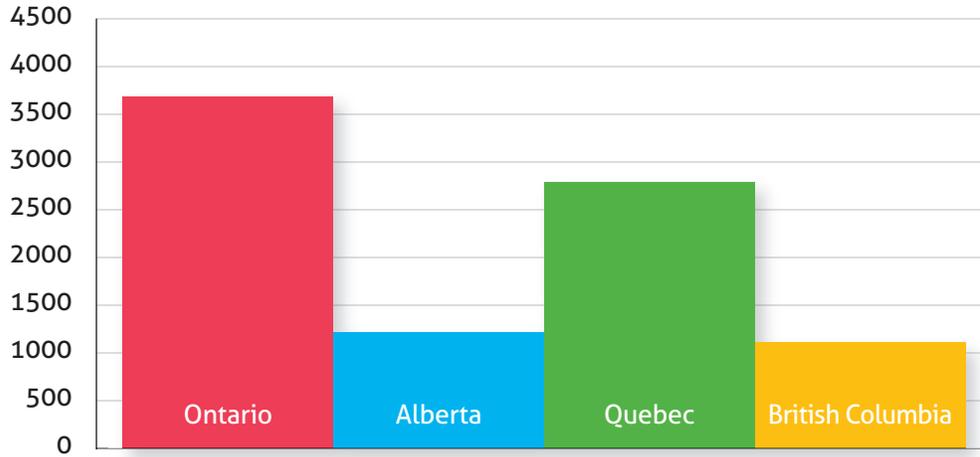
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Figure 1 shows that Canada leads Germany, Japan, the United Kingdom, and the United States in the number of publications, calculated as a function of population, in neuroscience and behaviour.

Within Canada, Ontario is the clear leader in total neuroscience research publications (*Figure 2*) when compared to Alberta, Quebec, and British Columbia, although the differences disappear when calculated per capita.

Figure 2

**NUMBER OF PUBLICATIONS 2003–2007 BY PROVINCE:
NEUROSCIENCE AND BEHAVIOUR**



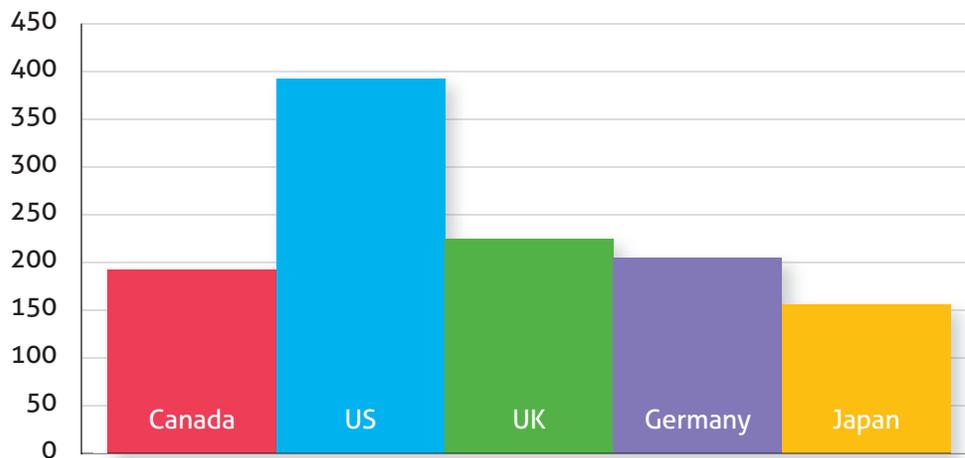
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Impact of publications

We also examined the relative impact of Ontario and Canada’s publications as compared to those in the United States, United Kingdom, Germany, and Japan. The h-index is a standard measure of impact and reflects the perceived quality of the research, taking into account both the volume and quality of publications for an individual, institution, or jurisdiction. In this analysis (*Figure 3*), the US is the clear leader, but Canada is highly competitive with the other world-leading countries.

Figure 3

**H-INDEX (1995–2007) BY COUNTRY:
NEUROSCIENCE AND BEHAVIOUR**



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Other data indicates that:

- Ontario is behind Massachusetts and Maryland, the site of NIH, in the number of neuroscience publications per million population, but the province ranks favourably with California, New York, and Pennsylvania.
- Within Canada, Ontario (at \$35 million) is second only to Quebec (at \$40 million) in the amount of annual funding for neuroscience research received from the Canadian Institutes of Health Research (CIHR).
- The “h” index of Ontario neuroscientists is behind that of some major centres in the United States, but is comparable to that of Quebec, and exceeds those of Alberta and British Columbia. When measured by city, “h” indices for neuroscientists in Toronto are similar to those of San Diego neuroscientists, but are behind their peers in San Francisco, Boston, and Philadelphia.

In summary, benchmarking indicates that of all the selected North American jurisdictions with strong neuroscience communities, Ontario by itself is currently competitive, but not a leader. Yet within Canada, Ontario is a leader in neuroscience output, with Toronto slightly behind Montreal as the country’s most productive centre.

Neuroscience in Ontario: Opportunity and promise

When taken together, data and information in this section indicate that brain research has made huge strides in the last 50 years. The field has advanced from understanding the molecular nature of the gene and the genetic code to decoding the entire human genome, and there have been parallel advances in brain imaging and in understanding how genes and environments interact.

These exciting advances in basic science have led to significant increases in our understanding of mental diseases, to the development of new treatments in neurosurgery, pharmaceuticals, and behaviour therapy, and to new market opportunities for drug companies and device manufacturers.

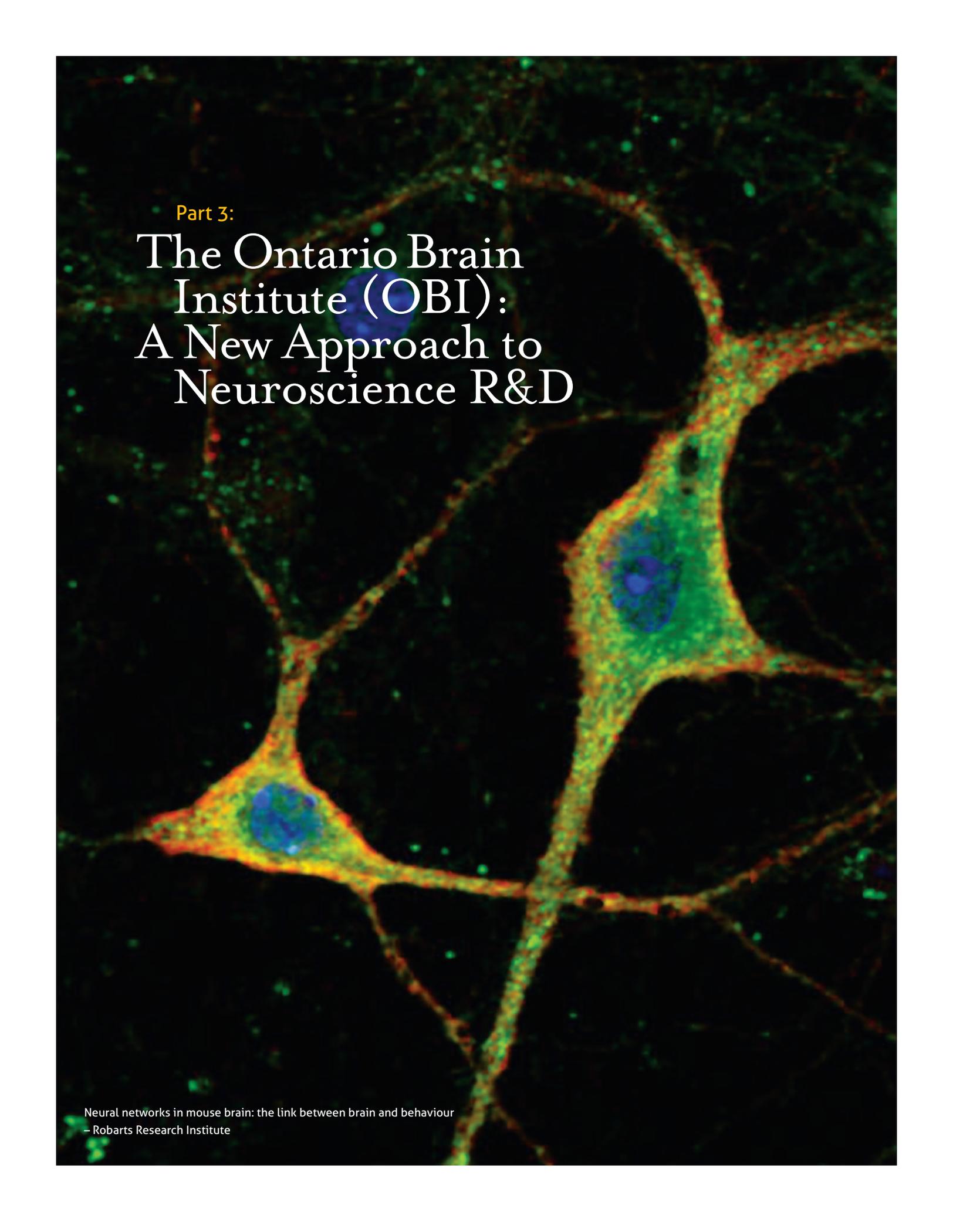
Ontario already possesses the elements necessary to become a world-class power in neuroscience in all three spheres — science, health care, and commercial development. But our excellence exists in pockets, and the province’s neuroscience currently lacks the integration of effort and focus necessary to achieve leadership status.

Because of Ontario’s historical strengths and the legacy of provincial investments already made, we now have the opportunity to marshal strengths, integrate efforts, and rise to the challenge.

The need now is for new incentives to:

- Bring the most accomplished scientists together.
- Break down institutional and disciplinary silos.
- Create structures to facilitate integration and stimulate breakthroughs in science.
- Encourage translation of new discoveries to clinical practice.
- Create opportunities for commercial development.

This truly unique coming together of talent around shared goals will transform Ontario into an international leader, competitive with the very best in the world. How can all this be brought about? We make some concrete suggestions in the next section.



Part 3:

The Ontario Brain Institute (OBI): A New Approach to Neuroscience R&D

ONTARIO BRAIN INSTITUTE (OBI) VISION:

Ontario is a world leading centre for brain research translation and innovation

Burden of Health and Social Costs
Scientific Revolution
Global Market Potential

FOCUS

Lifespan approach

- Developmental brain diseases, including early intervention in psychiatric diseases
- Neurodegenerative brain diseases (Alzheimer's, Parkinson's, and others)

ONTARIO BRAIN INSTITUTE

TRANSLATION: RESEARCH APPLIED TO CLINICAL CARE

A unique model of collaboration among Ontario's best current and newly recruited talent

- Cross discipline (basic and clinical)
- Cross institutional (a newly created central hub interacting with existing spokes)
- Industry (a valued partner)
- Training programs for scientists and physicians

SYNERGY

- Leverage previous provincial investments
- Stimulate commercialization based on discovery
- Tap into a huge worldwide market

OUTCOME

- Improved treatment for brain diseases and disorders
- Improved quality and efficiency of health care
- Lower social costs
- Ontario a global leader in translation of brain research
- Increased ability to recruit and retain top talent
- Greater capitalization of commercial opportunity, generating high value jobs and economic impact

HEALTH, SOCIAL
AND ECONOMIC
BENEFITS

CREATING THE ONTARIO BRAIN INSTITUTE (OBI)

As described in earlier sections, diseases of the nervous system have major adverse impacts, both societal and economic. Moreover, while Ontario's academic neuroscience research is fully competitive internationally, the science is not being commercialized effectively, and this represents a lost opportunity for wealth creation in the province. To meet this tremendous and growing need, we must accelerate the pace of neuroscience research. Even more importantly, we must come up with entirely new approaches to research in neuroscience, creating synergies between basic and clinical scientists, breaking down the barriers that separate disciplines, and working together with industry as a valued partner.

To become a world leader, OBI cannot study all aspects of brain function. Rather, it must focus on what it can do best. For that reason, we strongly advocate focusing on a set of related diseases and disorders, thereby encouraging interactions among scientists and increasing the probability of discovering effective remedies across clinical conditions. The appropriate focus for Ontario, is **lifespan brain development** — the development of the brain and CNS in infants, children, and younger and older adults. To respond to this need for action in this area of translational research, we recommend that the province commit to a bold new endeavour in brain research by establishing a new institute, tentatively titled the Ontario Brain Institute (OBI). The OBI's operations will be guided by four main principles:

1. **To study the brain during each of life's developmental stages**, focusing on developmental disorders of the brain and neurodegenerative diseases. During the early years of life, many psychiatric diseases become apparent, while others have their genesis but remain undetected. Thus, it is vital for OBI researchers to study brain development in children and adolescents; aging adults will also be studied, for it is they who develop dementia and degenerative neurological diseases such as Alzheimer's disease and Parkinson's disease.
2. **To stimulate translational research through scientific collaboration.** The OBI will entail a unique coming together of Ontario's best academic scientists and physicians, working hand-in-hand with industry and the provincial government. This partnership of professionals with varied skill sets and with access to patients afflicted with a wide variety of nervous system diseases will foster a high degree of interdisciplinary interactions to help ensure the translation of the best ideas to clinical care for patients.

“The neuropsychiatric disorders may affect a vast number of the population, they are the most mysterious, they are going to tell us much about the normal human brain. We are convinced that new knowledge will create breakthroughs in this field.”

— Dr. Martin Raff, Professor Emeritus of Biology, Medical Research Council
Laboratory for Molecular Cell Biology at University College London

3. **To create a training program in interdisciplinary neuroscience.** The goal of this program will be to expose young clinical investigators to in-depth basic science approaches, and basic scientists to the unsolved clinical problems faced daily by clinicians dealing with their patients. As a result, Ontario will become known as a centre of translational medicine for young scientists who seek to overcome the barriers of traditional disciplines.
4. **To build on the success of Ontario’s prior investments in brain research.** Ontario is already recognized as a centre of excellence in a number of diverse areas of neuroscience, many of which will be relevant to the major themes of the OBI. The Institute will bring together researchers from Ontario’s academic research centres in innovative programs, and recruit experts who will bring entirely new technologies to the province. The OBI will seek to partner with the Ontario Institute for Cancer Research (OICR), leveraging its strengths in genomics and other areas, and sharing expertise, new technologies, and ideas. Combining these strengths will inevitably increase the depth and reach of the research programs of both OICR and OBI.

We believe that, taken together, this new way of doing brain research, discussed in detail below, will result in scientific advances that would not come from scientists working alone. These advances will compress the time it takes to move discovery to innovation, accelerate the pace of progress in effectively treating diseases of the brain and nervous system, and ultimately alleviate the hardships of brain disease patients and their families.

The new OBI will ensure that Ontario realizes the full impact of its neuroscience research investments — indeed, its very structure (described below) is oriented to achieving this potential:

- Through its scientific focus, OBI will ensure that Ontario is investing in the areas in which we can truly excel.
- By fostering collaboration, OBI will ensure that its science is informed by the needs of patients and the health system; this collaboration will help Ontario harness the full potential of its researchers, health professionals, policy-makers, and entrepreneurs in advancing, translating, and applying brain science for the benefit of patients and their families and society at large.
- By leveraging its existing investments, OBI will ensure that Ontario efficiently deploys its resources, achieves on a globally competitive scale, and attracts new partners, philanthropists, and investors.
- By emphasizing translational science, OBI will support commercialization, strengthen local companies, and connect excellence in research with health and commercial dividends — ultimately leading to a world-class neuroscience industry cluster in the province.



Courtesy of Children’s Hospital of Eastern Ontario

PRINCIPLES GUIDING THE ONTARIO BRAIN INSTITUTE

Principle 1: To study the brain during each of life’s developmental stages, focusing on developmental disorders of the brain and neurodegenerative diseases

First and foremost, we recognize unequivocally that the OBI’s research director and the scientists participating in the Institute must set the precise research agenda of OBI, so as to reflect the opportunities and challenges they see in the ever-changing landscape of neuroscience research. For that reason, no attempt will be made here to proscribe specific research projects or approaches. However, our analysis of neuroscience research in Ontario and our insights gleaned from visits to other world centres for neuroscience research as well as local and global industry leaders, suggest that two broad areas are particularly ripe for scientific focus by OBI’s neuroscientists:

- Developmental disorders of the brain, which give rise to mental disorders — a foundational area at the leading edge of brain research.
- Neurodegenerative diseases, including Alzheimer’s disease, Parkinson’s disease, and stroke-induced dementias, a research domain in which Ontario is among a small group of world leaders.

We believe that these two areas should not be thought of as separate categories but as major aspects of a lifespan approach to brain development. In this sense, brains of newborn infants reflect not only their genetic inheritance but also influences from their mothers’ physical and mental environments while pregnant. As detailed in following sections, mental disorders of middle and later childhood can very likely be diagnosed and treated earlier than they are at present. Similarly, diseases and disorders of adulthood may be detectable well before obvious signs and symptoms appear. And many clinical researchers now believe that the neurodegenerative conditions of old age such as Alzheimer’s disease and Parkinson’s disease exhibit biomarkers, the use of which would allow diagnosis and treatment in mid-life. The lifespan approach will also allow the effects of various environmental variables — in the womb, in early and later childhood, and indeed throughout adulthood — to be measured, tracked, and assessed. The potential benefits of this integrated view of development are enormous.

(a) Developmental disorders of the brain

In assessing the state of neuroscience worldwide, our most troubling realization was that the understanding of the mechanisms underlying neuropsychiatric disorders is at best rudimentary. No one yet knows how these disorders arise, what causes them, and why some individuals and not others contract them. Furthermore, it is clear that such conditions develop within affected individuals, including children and adolescents, well before they become evident behaviourally. Thus, understanding the developmental causes of mental disorders is a central challenge facing brain researchers — and one that presents the greatest and most exciting opportunities for major breakthroughs given the technological advancements now available to us.



“The study of the neurodevelopmental disorders is where there’s going to be a research explosion; we can taste it. It may not be an Ontario strength yet, but it’s not a strength anywhere yet.” — **Dr. Michael Greenberg**,
Nathan Marsh Pusey Professor of Neurobiology and Chair of the Department of Neurobiology at Harvard Medical School

A true understanding of mental disorders will derive only when we fully understand the fundamental principles of brain development. This knowledge will be gained from investigating brain genetics and the functions of the genes we inherit from our parents, and also from more fully probing epigenetics, the effects of environmental factors on normal and abnormal brain development.

For example, recently discovered gene abnormalities contributing to disease include:

- Mutations in genes involved in the growth and regulation of crucial nerve cells that have been implicated in the abnormal brain development occurring in autism spectrum disorders.¹⁹
- A form of mental retardation, Angelman Syndrome, that may be due to the loss of a gene that regulates synaptic plasticity, the brain's mechanism for changing the strength of signals between nerve cells in response to high brain activity and the learning of new information.²⁰

Evidence for epigenetic control of behaviour comes from:

- Studies showing the abnormal expression of a gene regulating the utilization of hormones in the brains of childhood suicide victims who had been abused, as compared with brains of non-abused controls.²¹
- Evidence that infants raised in supportive and enriched social environments develop vocabularies and other mental abilities that are superior to those of children raised in non-enriched environments. These differences in vocabulary persist throughout life, with low vocabularies linked to such negative effects as poor school performance and reduced self-esteem. In the end, both the person and society lose.



Studies such as these emanating from Ontario's scientists and clinicians would be of enormous interest to medical caregivers as well as to Ontarians raising young children who are at risk for mental disease or who show signs of these diseases early in life. The identification of early biomarkers of psychiatric diseases could lead to the development of diagnostic procedures and devices for use in the clinic. Such a research enterprise could also result in therapeutic interventions involving pharmaceutical and other companies. Finally, if the critical features of beneficial childhood environments could be identified and verified, this knowledge could be translated into procedures and devices recommended for adoption in educational and domestic settings.

A number of additional reasons justify studying the origins of mental disorders:

- Understanding how the normal brain works will derive from understanding the abnormal physiology of brain disorders that alter brain function at various stages of development, from the very young to the aging and elderly.
- Defining the precise causes of mental disorders will help us to better categorize and differentiate the plethora of diseases now bundled under broad and misleading labels. For example, mental disorders are typically characterized by behavioural rather than pathophysiological criteria. Measured by behavioural criteria, a term like “schizophrenia” probably describes a number of diseases with very different anatomical and molecular origins. Understanding the precise pathological causes of mental diseases is thus an essential first step in differentiating them and in developing targeted therapies for their treatment.
- Understanding the pathology of mental diseases may well lead to the discovery of biological and diagnostic markers for early detection in the young, to enormous benefit. In autism, for example, behavioural therapy can greatly enhance social, motor, and cognitive skills, and therapy during early childhood produces the best results. The reason is that synaptic connections between nerve cells are “plastic” (i.e., can be modified by learning and repetition) which can ultimately alter behaviour. Also, certain genotypes predispose children to autism. Thus, genetic screening together with early therapeutic intervention could dramatically improve these children’s life experiences, with lasting effects through adulthood.
- In the face of our current dearth of information, it would be enormously valuable to fully understand just one mental disease: the molecular basis of cellular changes, how these changes alter normal brain development, and how therapies, both chemical and cognitive, can change the course of the disease. The lessons learned through a full understanding of this one disease could be extremely valuable as a prototype for understanding how other mental diseases arise and how they can be treated. With the research tools now available to us, this possibility can become reality.

(b) Neurodegenerative diseases

The numbers are staggering: every 70 seconds, someone in the world is diagnosed with Alzheimer’s disease. In the United States, where population analyses are available, 1 in 68 people have Alzheimer’s disease, accounting for 4 million people nationwide. In all, 3% of people between the age of 65 and 74 have Alzheimer’s disease, more than 50% of people 85 and older have the disease. Furthermore, more than 50% of Alzheimer’s disease patients are being cared for at home, which represents not only a major burden for the families providing care, but also for society, through massive increases in medical costs and lost productivity.

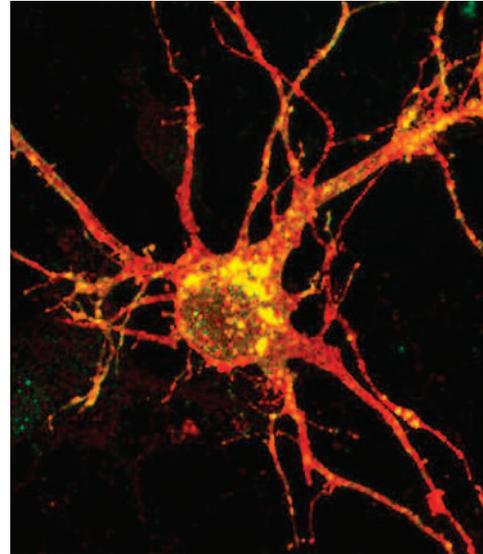


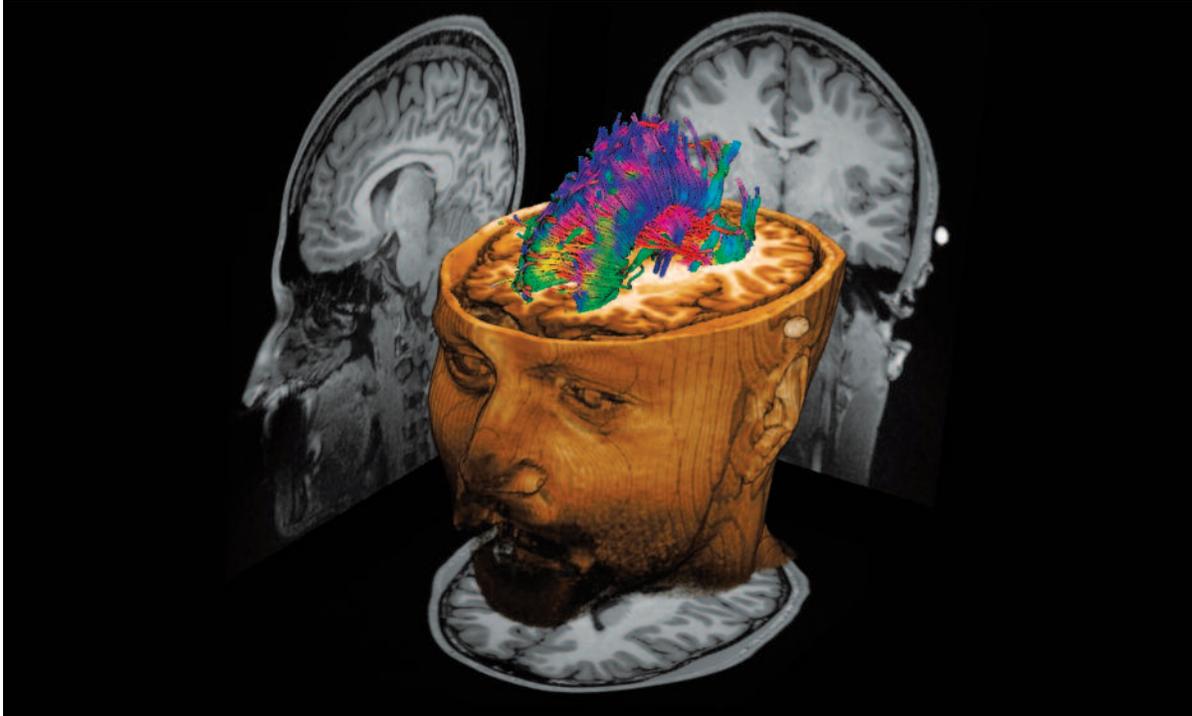
The brutal truth is, although we know much about the pathology of Alzheimer's disease, Parkinson's disease, and stroke-induced nerve cell death, there is little we can do to cure any of them. Solutions will come about only when we understand much more about the fundamental biology of nerve cell life, death, and regeneration.

We also need to know much more about the synapse, which connects nerve cells and controls their activities; about the influences that promote nerve cell repair; and about the recruitment of stem cells in certain parts of the brain that have the capacity to replace nerve cells that have died. As described earlier, Ontario's basic neuroscientists are already recognized as among the world leaders in the field of neurodegenerative diseases, so this initiative will significantly amplify and expand the breadth of established research excellence within the province.

We know that curing or preventing these diseases will require multiple approaches. For example:

- Ontario's geneticists and molecular biologists have made major inroads into the study of the amyloid- β protein (A β), which plays a key role in the nerve cell death and memory loss associated with Alzheimer's disease. But we do not know which biochemical pathways involved in memory are involved in amyloid-induced destruction of synapses or whether the changes in biochemical pathways that account for the impairment of cognition in the short-term (minutes to days), are the same pathways that lead to the death of neurons over weeks and months.
- Developmental neuroscientists will be key to discovering how neurons become specialized, how they change over time, how they form networks, and what makes certain networks more vulnerable to disease at different life stages than others (e.g., why does schizophrenia begin in the teens, and Alzheimer's disease in later life?). Furthermore, comparing developing and aging brains will be critical, since the same factors that induce normal nerve cell pruning in the developing nervous system of infants and children appear to be critically involved in the neuronal death occurring pathologically in Alzheimer's disease.²²
- Physicians who are working to reduce the occurrence of cerebral vascular incidents and treating patients who have suffered them will be crucial for these efforts since neurodegenerative diseases may also arise secondarily as a result of minor strokes.
- Cognitive neuroscientists will also play critical roles, for they evaluate normal aging and "super-aging" in both health and disease, including the concept of "cognitive reserve," the notion that the buildup of "cognitive assets" protects some people from the onset of neurodegenerative diseases.





Nerve tracts connect deep brain structures to the cerebral cortex – Roberts Research Institute

Principle 2: To stimulate translational research through scientific collaboration

Jurisdictions worldwide have tried to create centres of research excellence in medical research and biotechnology, but only a few (e.g., Boston, San Francisco, and San Diego) have been successful. For example, Boston and San Francisco have successfully marshalled their resources to emerge as easily identified world centres in neuroscience research. The reasons are multiple, (and perhaps even predictable): most jurisdictions lack a critical mass of basic and clinical scientists, and moreover, the scientists working in them fail to interact, with everyone continuing to pursue his/her own research interests rather than problems of common interest.

The question is, can Ontario overcome these problems and succeed where others have failed?

We believe the province can, and that the solution lies in implementing three strategies:

- 1. Creating a critical mass of basic and clinical neuroscientists across the province who closely interact with one another.** Ontario already has a network of first-class universities and research institutes with basic and clinical neuroscientists who are expert in their fields. Ontario's clinical neuroscientists are highly skilled professionally and have access to a large and diverse population of patients with diseases of the nervous system, providing the clinical problems and materials for studies aimed at understanding disease of the nervous system. Also, Ontario's basic scientists have access to many of the latest technologies and tools for investigating the brain and other parts of the nervous system, technologies that will allow OBI to do things differently and that will serve up scientific opportunities never before available.

The clinical and basic neuroscientists with whom we spoke in Ontario recognize the huge potential of collaborating across fields and disciplines. They are eager for professional interactions with colleagues in different fields, and they are enthusiastic about dissolving the “silos” that have traditionally separated disciplines, departments, and institutions. They recognize that their own projects and interests can benefit from the expertise of others, and that they, too can contribute in entirely new ways to the work of their colleagues.

The National Academy of Sciences in the United States has recognized the importance of collaboration in the field of neuroscience. Their 2008 workshop report — From Molecules to Minds — described the importance of collaboration as follows:

“Recognizing that neuroscience is not, of course, really a single field is important. Rather, it is a multidisciplinary enterprise including diverse fields of biology, psychology, neurology, chemistry, mathematics, physics, engineering, computer science, and more. If scientists within neuroscience and related disciplines could unite around a small set of goals, the opportunity for advancing our understanding of brain and mental function would be huge.”

- 2. Consolidating Ontario’s clinical and basic neuroscientists around a fixed number of research goals that are competitively reviewed and milestone driven.** To be successful, the OBI will need to first identify a small number of research goals, and then marshal the talents of key members of the initiative to decide upon the strategies to be used to achieve them. In other words, the initiative’s model needs to be different from that of traditional, academic, curiosity-driven research in which investigators are evaluated by the number and quality of their research publications accepted by the best journals. Scientific publications and the ability to attract external funding will count, but for the OBI, scientific contributions to the shared goals of the Institute should be the yardstick against which progress and the value of an individual investigator’s contributions are measured.
- 3. Working in partnership with industry and government to achieve shared goals.** In addition to funnelling new technology and discoveries to industry for commercial development, (i.e., the traditional mechanism for translating academic research into the market place,) the OBI will embrace industry as a full partner in this effort. Wherever possible, industry scientists will be encouraged to interact with OBI scientists, to participate in problem solving, to identify and advise on projects with true commercial value, to contribute knowledge and technology to achieve shared goals, and to remain informed about progress, problems, and challenges within the OBI.

OBI will also work closely with the province to keep it and the citizens of Ontario informed of progress, and it will work with policy-makers to reinforce Ontario’s world image as a visionary province dedicated to intellectual pursuits and to the creation of new knowledge.

Principle 3: To create training programs across neuroscience disciplines

The future of translational science lies in the hands of the new generation of physicians and basic scientists who are becoming increasingly driven to answer questions of clinical relevance. Young physicians, MDs, and MD/PhDs, recognize that to understand the disease behind the symptoms they treat, far more needs to be known about the basic biology of the brain and its diseases. They also realize that to contribute in this sphere, they need the specialized scientific training that will allow them to probe important fundamental questions. Conversely, basic science graduate students, PhD students, and postdoctoral fellows are eager to have their research improve the lives of patients, which will require them to become familiar with problems in clinical medicine and to work closely with physician colleagues.

The OBI, working with its university partners, will serve all of these trainees by creating a well-funded training program in which student mentorships will be provided by basic and clinical investigators working together on shared problems, encouraging exchanges between clinical and basic science laboratories, and creating joint projects on which young physicians and PhD scientists will collaborate. In addition, programs will be established to cover salaries of clinical trainees who will be spending time away from their clinical duties.

The success of this program will attract the best physicians, clinicians, and basic science trainees to Ontario, many of whom will want to stay within the province once their training is completed. In doing so, it will reinforce Ontario's reputation as a world centre uniquely focused on mobilizing discovery research towards patient care and translational neuroscience.

“We’re interested in understanding and improving brain health. And that means not just solving the disease but preventing it. Understanding enough so that you can diagnose it early enough so you can nip it in the bud.” — **Dr. Terrence Sejnowski, Professor and Head of the Computational Neurobiology Laboratory, Salk Institute**

BUILDING ADDITIONAL RESEARCH STRENGTHS

A number of “platform technologies” essential for the proposed research program are currently either not easily accessible or, in some cases, not available at all to Ontario’s neuroscience community. As a result, significant technological requirements still exist, and commitments must be made to shore up these platforms to enable the province’s neuroscience research to be internationally competitive. These technologies should be established, subject to the scientific needs of the network and the research directions chosen by leadership and network scientists.

Specific platform technologies might include:

1. Optogenetics. Access to optogenetic methods, mentioned earlier, will be key to mapping neural pathways in complex systems. These recently developed techniques, with more sophisticated technologies certain to come, allow neuroscientists to introduce into neurons genes and viruses that carry detectable markers for nerve cell labelling. This permits monitoring the interconnections of nerve cells across synapses and different regions of the brain. Also needed are non-invasive ways to image the activity of single molecules within defined regions of cells of interest.

In addition, methods that control the activity of specific nerve cells within the brain using light stimuli to activate membranes of neurons (discussed above) will be of significant value in understanding the roles of specific neurons within nerve tracts of interest. As an example, a recent study²³ has shown how this technique can be used to assess the circuits involved in deep brain stimulation-induced tremor reduction.

Carrying out optogenetics will require access to the latest technologies in single and multiphoton microscopy, highly sophisticated instruments that will need to be maintained by expert microscopists, who can make them available to more casual users, including trainees, within supervised core facilities.

Clearly, we are at the beginning of a revolution in microscopy as it relates to brain function. High-resolution dynamic microscopy with the capacity to evaluate single molecules all the way up to whole brain regions will be an essential tool in the effort to understand how complex heterogeneous nerve cell networks systems function in normal and diseased brains.

2. Neurogenetics. OBI will need to expand the neurogenetics expertise of the province to carry out genome-wide association studies of high-risk populations leading to the identification of genes associated with various diseases, and to the genetic analysis of specific patients. Personalized genomics is now possible, given the ever-decreasing cost of high-volume gene sequencing and the rapid development of new-generation gene sequencing methods. Given the fundamental importance of genetic technology to understanding brain diseases, a vibrant neurogenetics program will also be the foundation upon which to build links between Ontario and other neuroscience centres around the world.

The neurogenetics program will require the support of a bioinformatics core facility to process the information it generates as well as a high performance computer centre, which will be involved in both data capture and in the model building carried out by computational neuroscientists associated with the OBI.

3. Sleep and circadian rhythms. One research area in which Ontario already has strengths, but in which the province, by enhancing its capacity, could further distinguish itself internationally in support of its research priorities, is the generally understudied area of sleep and circadian (24-hour day-night) rhythms. The area is emerging as a major factor in neuroscience research for a number of reasons:

- Circadian timing is a pervasive feature of all human tissues, including the brain, with up to 10% of all genes in any one tissue under circadian regulation as measured over 24 hours.
- Because physiological processes change over the circadian cycle, an individual will be more or less prone to illness at different times of day, and therapeutic efficacy will vary. For example, acute cardiovascular and cerebrovascular episodes, including stroke, are more common in the morning, when circadian mechanisms increase both cardiac output and susceptibility to thrombosis.
- Sleep has a major influence on the immune system. One sleepless night can reduce populations of key disease-fighting cells by 28% and raise by 50% levels of hormones that inhibit the immune system. Mental health and neurodegenerative diseases are almost always associated with disturbances in sleep, and sleep-maintenance insomnia and early-morning awakening are hallmarks of major depression.

In short, understanding the mechanistic links between sleep and circadian rhythm disruption in mental health and neurodegenerative disease could foster the development of biomarkers and evidence-based diagnostic criteria. It could also lead to improved treatment guidelines for sleep pathologies in these patient groups.

4. Molecular neuropathology. OBI will need to provide network scientists with the ability to analyze genes and gene products within specific tissues and cells. Molecular neuropathologists provide this technology in a number of ways using technologies to monitor specific genes and gene products in tissues from brain banks, patient biopsies, and samples from experimental animals. In addition, laser-capture microdissection can be used to monitor the molecular changes in one or more cell types in normal and diseased tissues. Having access to these highly sophisticated methods will greatly expand the reach and elegance of the studies done by OBI scientists and will also enhance the penetration of the scientific questions they are able to ask.

FACILITATING ONTARIO'S COMMERCIAL OPPORTUNITIES

1. Drug, device, and business development. One of the functions of OBI will be to stimulate the commercial development of neuroscience products and technology in the province. For that reason, the hub should provide platform technologies and resources that add scientific value to technologies before their spin-off or licensing, thus strengthening the “proof of concept,” which in turn will facilitate the commercialization process.

For technology transfer to be seen as a priority within the network, OBI should support the research of its faculty in several ways neither generally available to scientists nor well done in

traditional academic settings. For example, OBI should hire a drug development scientist who has worked in industry to lead efforts to bring new molecules to commercial development. He/She should have the ability to analyze compounds and to partner with other specialists or consultants in further molecular development.

OBI should also employ a strong project manager to help scientists develop project plans and work to help them to achieve research milestones. The key will be to develop the right plans up front, and to identify at each stage of the pre-clinical and clinical processes those end points needed to make the difficult go/no-go decisions as early as possible. Scientific support will include creating partnerships with industry or contract research organizations (CROs), for example, to develop drugs that are analogous to natural products, and to carry out toxicology studies to test safety and effectiveness. To help put these critical partnerships in place, OBI will work in collaboration with MaRS, which has taken on a leadership role in interacting with the network of university commercialization offices across the province.

2. Clinical trials office. Once a candidate drug, device, or diagnostic instrument is close to clinical application, OBI will begin building the necessary clinical infrastructure to support it, including hiring a senior development manager (a medical doctor with clinical development expertise). That person will design and manage the trials with CROs and industry partners and be responsible for reviewing the data, interacting with regulatory agencies, and writing reports. Others who might be hired as permanent faculty or as consultants to specific projects include chemists, engineers, physiologists, computational biologists, and bioinformatics specialists. The development manager would also work with the province in establishing the patient registries necessary for additional, more advanced clinical trials.

The OBI will provide neuroscience expertise, client focus, and provincial sector coordination, working in concert with the commercialization “mesh” network currently evolving in Ontario.

Not only will the creation of the business development and clinical trials resources within OBI (working in partnership with the regional commercialization network) accelerate neuroscience commercialization in the province, it will also assist in addressing the needs that have been identified to enhance the commercialization of advances in neuroscience technology, including:

- Increase in patent activity and technology licensing agreements.
- An increase in the technologies brought to market.
- Attraction of multi-national industry investment in the province.

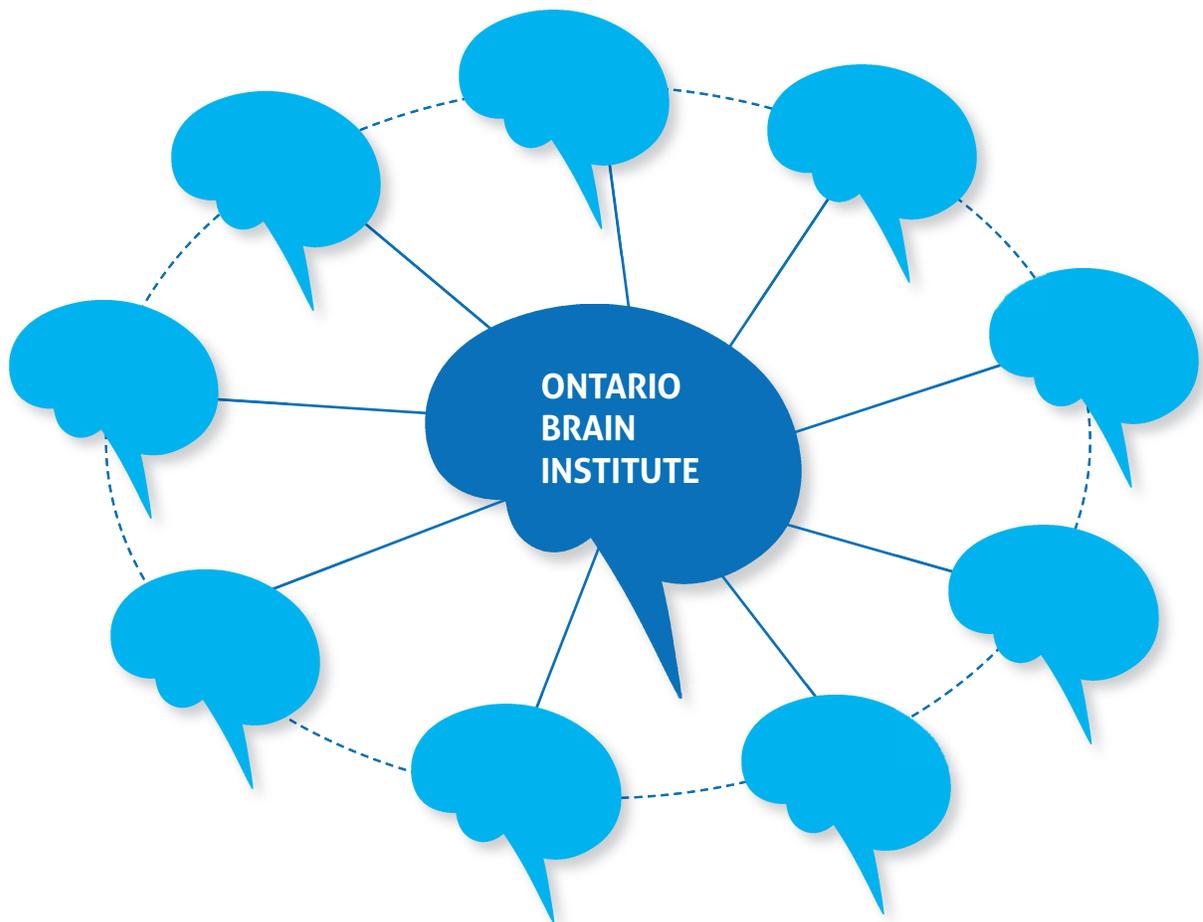
In summary, the OBI, by positioning Ontario to make significant contributions to global brain research; by improving standards of care for those at risk for or afflicted by brain diseases; and by fostering a vibrant, discovery-driven commercial cluster, will propel the province into one of the world’s leading centres for translational brain research and innovation.

STRUCTURE OF THE ONTARIO BRAIN INSTITUTE

Hub-and-spoke organization

OBI needs to be organized as a network that

- Facilitates the interactions of Ontario's most outstanding neuroscientists across the many research centres,
- Focuses on cross-disciplinary and translational research involving collaboration between basic scientists and clinicians,
- Sets common research goals and establish strategies for achieving those goals,
- Sets milestones for measuring progress,
- Recruits new scientists and trainees to Ontario to participate in these efforts,
- Works comfortably with industry partners with the knowledge and ability to fast-track discoveries to the marketplace,
- Works together to reduce the time it takes for laboratory discoveries to translate to improved patient care,
- Provides central support and resources, and enables better integration of regional institutional efforts,
- Partners with existing programs to create synergies and avoid duplication.



In our view, OBI can most effectively achieve these ideals by employing a hub-and-spoke model similar to that adopted with great success by the OICR, one that will provide strategic focus for Ontario's existing and anticipated strengths.

The hub (i.e., the central organizing facility for the OBI network) should be located in a neutral site not affiliated with a current Ontario university; the MaRS building in Toronto would be an ideal setting. The director, located in the hub, will be the network's central organizer, working with an external advisory committee of international scientific experts (Scientific Advisory Board (SAB), see below) and OBI scientists to create research programs and goals, set milestones, monitor progress, and lead faculty recruitment.

Ideally, the director will be a visionary, inspirational and energetic leader who is also an active scientist, with international connections and networks, and highly motivated towards the goals of OBI. The director should also be generous in spirit towards members of the OBI, recognizing the importance of everyone's contributions to the success of the initiative. The director, guided by the SAB, will also recruit to the hub scientists who are expert in those platform technologies not currently available in the province — technologies that can support the work of others in the network.

Multiple spokes consisting of participating scientists within Ontario organizations will be located in Ontario's most research-intensive universities and institutes, each spoke led by an outstanding senior scientist who will recruit additional faculty members to his/her organization, in agreement with the OBI director. The spokes and their leaders will be identified by the scientific director who will meet with potential candidates, discuss research priorities, and then issue requests for applications that will be evaluated by external peer review. The leaders and program PIs will be the most productive, dedicated, and creative neuroscientists presently within Ontario whose interests fit with the priorities of the OBI, as well as excellent scientists to be attracted from outside the province who will bring new technologies and ideas into the program. Funds for the OBI's strategically focused programs will be distributed to researchers within the hub and spokes, based upon rigorous peer review by an external scientific review panel.

The SAB should be established to advise the OBI and monitor its progress, including evaluating programs and the progress made towards research goals (using peer review). The SAB should also advise the OBI Board on the effectiveness of the research director, whose skills at bringing people together and at defining shared goals and strategies will be essential to the program's success.

OBI should also set as a high priority the establishment and funding of an interdisciplinary training program for postdoctoral students, and work with the universities to extend this program to graduate students and physicians, with the goal of providing the next generation of neuroscientists with the highest quality training. This will entail providing clinician scientists with the time, salary, and opportunities to expand their research portfolios, and providing basic scientists with adequate exposure to clinical problems to help them translate their research to clinical applications.

To ensure truly interdisciplinary training, basic scientists and clinical investigators should jointly mentor trainees, thereby ensuring that cutting-edge science will be applied to clinical problems, and that important and appropriate clinical problems are explored in the laboratory.

Synergy with the Ontario Institute for Cancer Research

We believe that OBI can benefit from the experience and resources already invested in the OICR. For example, OICR is heavily invested in genomics for cancer as well as in drug development, pathology, biochemistry, and molecular biology. OICR faculty members have neither the time nor the expertise to carry out these functions for OBI, but bringing together faculty members from both programs — perhaps working in separate sections of the MaRS building (see below) — would create a powerful critical mass of research talent engaged in sharing ideas, expertise and equipment, and, as appropriate, in facilitating the application of discoveries made in one program to the other.

The advantages of such research interactions among the scientists of both institutes would extend to all researchers across the province involved in the institutes' programs.

SCOPE AND SCALE OF INVESTMENT

The OBI will function through a hub and spoke model, and each component will require initial setup funding for equipment and annual funding thereafter for operating support, training, special projects, and equipment renewal. Funding will need to be controlled by the OBI's director, subject to the peer review mechanisms established by the OBI's Scientific Advisory Board.

Many questions will need to be answered before a precise budget can be constructed for the OBI. For example, if the hub is to be located in the MaRS building in Toronto, which would seem an ideal location, rent would be based upon the space utilized, which in turn would depend upon the number of investigators and trainees onsite.

To create a critical mass of talent along with associated technologies, one might expect 15 to 20 investigators plus the research director to be housed in this central location. Providing new equipment and setup monies for each of these individuals would be essential. Additional expenses will also be incurred within the hub to support OBI's central administrative offices, including those for business development, fundraising, public relations, and public education, among others.

Additionally, each of OBI's scientific programs will require one research director with 3 to 5 co-investigators, preferably but not necessarily at the same institution. Some co-investigators will already be present in the Ontario system, but others will need to be recruited. Recruiting new faculty members will require a budget of approximately \$1 million per investigator, and operating support will need to be provided for all investigators working in each program. In addition, money as well as equipment will be required during initial setup. The number of investigators and the operating budgets for each would be determined by the nature and requirements of the science being conducted.

We expect that many projects created within the OBI will be supported by government funding agencies such as CFI, CIHR, and NIH, as well as disease-oriented private philanthropic agencies such as the National Alliance for Research on Schizophrenia and Depression, Autism Speaks Canada, the Alzheimer Society of Canada, and others. Major funding may also be forthcoming from philanthropists who are interested in diseases of the brain.

Until these and other details are worked out, the best estimates of a reasonable budget might be derived from analyzing the budgets of other research institutes with comparable missions. (Caution should be exercised in comparing the budgets of other organizations with that of OBI, however, since some but not all the comparators may include salaries for investigators and other costs that do not relate to the OBI). It is also important to recognize that annual research operating budgets are typically supported by a combination of funding, which includes philanthropy, endowment-based operating funds, PI research grants, and other sources. Below are some examples.

The Allen Institute for Brain Science houses 125 scientists in neuroscience, molecular biology, informatics, engineering, mathematics, statistics, and computational biology. It was established by a philanthropic gift of \$100 million, with additional funding coming from federal and state governments, private donations, and foundations.

The Stanley Center for Psychiatric Research in Cambridge, Massachusetts, was established with funding of \$100 million from the Stanley Medical Research Institute, with the goal of understanding the molecular underpinnings of bipolar disease, schizophrenia, and major depression, and to determine if molecular abnormalities can become viable targets for new treatments. The Institute is part of the **Broad Institute**, which was established by a \$400 million philanthropic gift that generates \$20 million in operating income per year. The total budget of the Broad Institute is about \$100 million a year, with the majority of funding coming from peer-reviewed research grants.

Cold Spring Harbor Laboratory is a private, non-profit research and education Institute located in Cold Spring Harbor, New York, with 730 employees, 400 scientists, and 70 senior scientists. The organization conducts research in four areas: cancer, bioinformatics, plant genetics and neurobiology, with 12 senior scientists working in neurobiology. Its annual budget is \$115 million, and its sources of funding are 34% federal grants, 32% other foundation grants, 17% endowment. Neurobiology accounts for 18% of the budget, or \$21 million annually.

National Institutes of Health (Institute of Mental Health (NIMH), Neurological Disorders and Stroke (NINDS), Drug Abuse (DA), Alcohol Abuse and Alcoholism (AAA): NIMH has 600 staff, 500 scientists, and 1000 trainees (\$158 million for intramural research and \$60 million for research management); NINDS has over 500 scientists (\$145 million for intramural research and \$53 million for research management); DA has 370 staff, 120 intramural researchers (\$82 million for intramural research and \$56 million for research management); AAA has 220 staff, 100 intramural researchers (\$46 million for intramural research and \$25 million for research management.)

Max Planck Society Research Institutes (MPI for Brain Research; MPI for Neurobiology; MPI for Neurological Research; MPI for Psychiatry; MPI for Human Cognitive and Brain Sciences): The Max Planck Society, a private, non-profit organization, operates 80 Max Planck Institutes and other research facilities across Germany, plus several abroad. Each MPI is an independent organization, linked to partner universities and hospitals through joint appointments, cooperation agreements, and graduate programs; many provide specialized major research equipment and facilities. Five institutes carry out significant neuroscience research. Pro-rating on the basis of senior scientists, each MPI receives about 60 million Euros annually (\$94 million CAD).

Salk Institute for Biological Studies: Located in La Jolla, California, the Salk Institute employs 57 faculty investigators and a scientific staff of more than 850. Neuroscience research, with 27 faculty, is one of three major areas of study (the others being molecular biology and genetics, and plant biology). Annual funding for the Salk Institute is about \$100 million, of which two thirds comes from the NIH and the balance from private foundations.

The McGovern Institute for Brain Research, associated with MIT in Cambridge, Massachusetts, is a neuroscience research institute committed to improving human welfare and advancing communications. A team of multi-disciplinary neuroscientists conducts integrated research in three broad themes — perception, cognition, and action — using systems and computational neuroscience, brain imaging and cognitive neuroscience, and molecular biology and genetics. The McGovern Institute was established in February 2000 by a gift from the McGovern family expected to total approximately \$350 million. The Institute's operating budget draws on this source, and also on externally funded government grants.

It must be noted that funding figures for these example institutions cannot be compared side by side. In some cases, the mandate of the organization extends beyond neuroscience research, and the nature of the funding arrangements among the institutions varies significantly. They do demonstrate, however, that the institutions rely on more than one funding source and that these evolve over time. Most are a mix of philanthropic support from foundations or individuals, funding from interested corporations, and public funds, either through competitive research grants or direct operating support funds.

The examples make it clear that various combinations of government, philanthropic, corporate, and granting council funds can be employed, first to establish a world-class research institute, and second to provide funds for ongoing infrastructure and research costs. In the case of OBI, however, it seems clear to us that government must take the lead investing in the new Ontario institute to ensure scope and scale at the world level. Without that leadership, the collaboration of disciplines and institutions will not happen, the initiative will not attract other sources of funding, and clinician-researchers will be reluctant to participate. However, with government commitment, the new institute will attract funds from private donors, charitable foundations, and such agencies as CFI, CIHR, and NIH.

It is also clear from comparable examples that funding will evolve over time, both in amount and composition. Large initial commitments are required to create the hub and its associated infrastructure and research platforms; ongoing operating costs will rely progressively more on granting councils. In our view, the final annual budget of the OBI must be at least \$100 million. This estimate is both reasonable and necessary if the OBI is to develop into a transformational force in international neuroscience. In the absence of such an investment, Ontario will fail to capitalize on its past infrastructure investments and on the talents of the superb neuroscience researchers and physicians working within the province.

POTENTIAL BENEFITS TO ONTARIO

In mobilizing Ontario's excellence in brain research under a common translational vision, the OBI will position the province to:

- (a) Make a significant contribution to global brain research.
- (b) Improve the standard of care for those at risk for or afflicted by brain diseases/disorders.
- (c) Foster the economic potential of a vibrant, innovation-driven neuroscience cluster, ensuring that Ontario realizes the full impact of current and future research investments.

A. SCIENTIFIC BENEFITS

Objective:

Ontario will be recognized internationally as one of the world's top-five jurisdictions for brain science.

OBI will provide Ontario's brain research community with:

- 1. Improved access to brain research expertise and resources now spread across the province.** The Institute will mobilize Ontario's brain research community, bringing new opportunities for dialogue and collaboration and much-improved access to the research assets (expertise, technologies, equipment) housed at institutions across the province.
- 2. Greater opportunity for global collaboration.** OBI will catalyze partnerships with leading global centres to enhance research and training capabilities and thus achieve greater impact.
- 3. Enhanced recruitment and retention of top talent.** OBI will help attract to Ontario from around the world the best and brightest scientists and clinicians interested in translational neuroscience medicine.
- 4. Unique training opportunities for cultivating the next generation of scientific and clinical leaders.** OBI will provide a learning environment that equips trainees with the research skills and cross-disciplinary understanding needed to make significant contributions to brain research and medicine.

MEASURING OBI'S SCIENTIFIC IMPACT	
SCIENTIFIC OUTPUT	<ul style="list-style-type: none"> • Volume and impact of publications • Amount of grant funding secured from external sources
TALENT	<ul style="list-style-type: none"> • Number of scientific and clinical leaders recruited • Number of graduate and medical students and fellows trained
GLOBAL RECOGNITION	<ul style="list-style-type: none"> • Number of international collaborations • Number of invited presentations/lectures

B. HEALTH AND SOCIAL BENEFITS

Objective:

Ontario will be a recognized world leader in the translation of brain health knowledge to improving the prevention, care, rehabilitation, and management of brain disorders.

Brain diseases are devastating for affected individuals; beyond the direct impact on patients' functional outcomes and their abilities to cope independently with daily living, afflictions can profoundly diminish quality of life, irreversibly alter patients' autonomy and sense of self, and accelerate the course of other co-morbid conditions. Furthermore, the economic burden of brain diseases is substantial in direct health system costs, indirect costs associated with premature departures from the labour force, and costs associated with growing demand for social programs. These costs will only increase with the growing prevalence of these afflictions.

In undertaking an innovative approach to understanding the healthy brain and brain diseases across the lifespan, OBI will provide researchers and clinicians with an unprecedented opportunity to collaborate in developing new approaches that will raise the standard of brain health care and reduce the economic impact of brain diseases on Ontario's health and social systems.

Anticipated health and social impacts include:

1. Discovery of new medical interventions. OBI researchers will generate new knowledge of brain development and the origins of disease that will, in turn, lead to evidence-based practice guidelines and innovative diagnostics, therapeutics, and medical devices.

“Ontario has an opportunity in this initiative to create an international competitive advantage in brain research.”

— Dr. Christian Fibiger, Senior Vice President and Chief Scientific Officer,
Biovail Corporation

2. Accelerated access to novel technologies. Mobilizing and coordinating the expertise needed to develop and test brain health innovations provides patients with access to the latest discoveries. By improving Ontario’s ability to coordinate clinical brain research (through streamlined administrative systems, access to technology and improved opportunities for collaboration), OBI will facilitate the sharing of resources on a much larger, province-wide scale and allow the healthcare system to benefit fully from Ontario’s investments in brain health innovation.

3. Reduction in the demand for social services. Through greater insight into neurodevelopment, OBI researchers will generate new approaches aimed at preventing and/or reversing the course of early-onset chronic brain diseases (such as learning disabilities, autism and psychiatric conditions) and neurodegenerative disorders (such as Alzheimer’s and Parkinson’s diseases). Future advances may well translate into prolonged independent living for patients having these diseases and reduced reliance on the social safety net.

4. Improvements in health system effectiveness. In pursuing a clearer neurodevelopmental understanding of the brain in health and disease, OBI will spur the development and testing of approaches to prevention, detection, and intervention that will usher in a revolution in care — extending our focus beyond the diseased brain and making protection of the healthy brain our foremost priority.

SAVING HEALTH CARE COSTS FOR ALZHEIMER’S DISEASE

Delaying the onset of disease

In the United States, the costs for caring for patients with Alzheimer’s disease is \$184 billion a year. A study has estimated that a preventative measure that could delay the onset of disease by five years would save **\$50 billion** in annual health care costs – a saving of more than 25%.²⁴

For Canada, a 25% savings in the costs of caring for patients with Alzheimer’s disease would amount to **\$1.4 billion** a year.²⁵

MEASURING OBI’S HEALTH AND SOCIAL IMPACT	
DISCOVERY AND DEVELOPMENT OF BRAIN HEALTH INNOVATIONS	<ul style="list-style-type: none"> • Number of new brain health technologies/practices • Number of clinical trials conducted by OBI investigators • Number of Ontario patients participating in clinical trials
IMPROVEMENTS IN PATIENT CARE	<ul style="list-style-type: none"> • Health policy/clinical changes arising from OBI research • Number of OBI discoveries adopted into clinical care • Number of clinicians affiliated/collaborating with OBI
BURDEN OF DISEASE	<ul style="list-style-type: none"> • Direct and indirect costs of treating brain diseases/disorders • Demand for social services by individuals afflicted with brain diseases/disorders

C. COMMERCIAL/ECONOMIC BENEFITS

Objective:

Ontario will be well positioned to capitalize on the commercial potential of its research, attract new investment, and create high-value jobs in the “neuro” industry.

In addition to developing and delivering innovation to Ontario’s health system, the province’s enhanced capacity in brain research will drive commercial activity (spin-off technology companies, job creation, private sector investment) and thus fuel the competitive growth of Ontario’s knowledge-based economy.

Through advancing a research agenda attuned to industry priorities, providing centralized access to commercialization-supportive platforms, and leveraging complementary investments aimed at facilitating technology development (e.g., MaRS and the OICR), OBI can catalyze the transformative growth of Ontario as a world-class neuroscience commercial cluster. The potential economic impact of such investment includes the following,

- 1. Increased private sector partnership/investment.** Access to a well-coordinated group of leading investigators and supporting research infrastructure will attract industry partnership throughout the R&D process, providing input that nurtures ideas with potential commercial impact (such as new drug targets, biomarkers, and animal models).
- 2. Improved technology transfer and commercialization.** OBI’s research output will create opportunities to add value to intellectual property, taking promising technologies to more advanced stages of development prior to out-licensing or spin-out, thereby supporting the creation of stronger, most sustainable companies.
- 3. Cluster growth.** Research excellence can seed the growth of a vibrant life sciences cluster that nurtures local start-ups and attracts investment from larger firms.

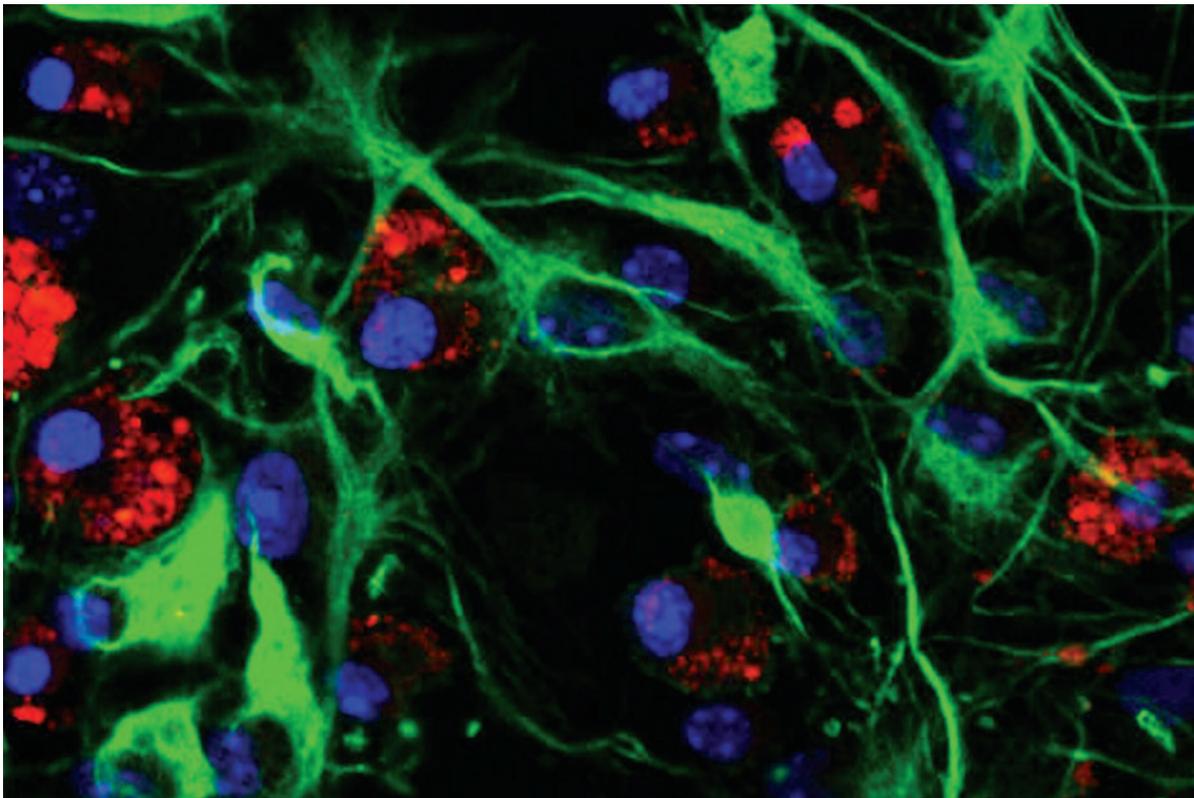
MEASURING OBI’S IMPACT ON COMMERCIAL DEVELOPMENT	
TECHNOLOGY TRANSFER AND COMMERCIALIZATION	<ul style="list-style-type: none"> • Number of patents • Number and value of technology licensing agreements • Number of technologies brought to market
CLUSTER GROWTH	<ul style="list-style-type: none"> • Number of companies created • Number of high-value, knowledge-based jobs created • Number of partnerships/collaborations (academia-industry; industry-industry) • Number of companies attached to Ontario • Value of private sector investment in brain research

CONCLUDING COMMENTS

Recent explosive advances in technology have permitted researchers worldwide to investigate the brain from many diverse perspectives with enormous implications for clinical practice. For example, methods are now available that permit scientists to

- Study genes and proteins that regulate nerve cell function.
- Monitor synapse activity that connects nerve cells one to the other.
- Trace the networks that nerve cells form to connect brain regions.
- Show how these networks interact to produce and regulate normal and abnormal behaviour.

Taken together, these technologies have enabled scientists for the first time in human history to believe they may some day understand how the brain's 100 billion nerve cells interconnect in intricate networks to regulate all aspects of human activity. This understanding will not only give us deep insights into what makes us human, but it will also provide us essential clues to understanding brain diseases, enabling us to translate new knowledge to therapies and cures of enormous benefit to patients, their families, and society.



Astrocytes and neurons – Robarts Research Institute

Inspired by the neuroscience technological revolution, governments worldwide are pouring money into brain research. Ontario is in an enviable position to seize the moment as well, for our province's universities, research institutes, and affiliated teaching hospitals hold a "critical mass" of world-recognized talent — superb professionals who are already benefitting from Ontario's significant investments in infrastructure and equipment. Yet most of these individuals work either alone or in small groups, and most are hampered by the traditional, if invisible, boundaries that separate academic disciplines and institutions. They could accomplish so much more by crossing these boundaries, combining their differing skill sets and approaches, and thus synergizing their efforts within an entirely new model of conducting medically relevant brain research.

The Ontario Brain Institute creates such a model by bringing together, within a network, the very best of Ontario's neuroscientists and physicians and their trainees to collaborate on important problems of common interest. Their joint studies will be grounded in:

- An effort to improve our understanding of the fundamental principles of brain development across the lifespan.
- A desire to translate that information to understanding the etiology of mental disorders and neurodegenerative diseases.
- A push to inspire industry to invest in the province to develop diagnostics, therapies, ancillary products, and eventual cures for patients.

Through the Ontario Brain Institute, the province will emerge as a world centre of excellence in neuroscience research, and potentially in the commercial development of medical products for brain diseases. And for the first time, Ontario's patients with devastating brain diseases will face the future with hope that is grounded in genuine progress.

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Appendices

APPENDIX 1: INTERNATIONAL SCIENTIFIC ADVISORY COMMITTEE (ISAC)



HUDA AKIL, Ph.D.

Dr. Akil is the Quarton Distinguished University Professor of Neuroscience and Psychiatry at the University of Michigan, and the co-Director of its Molecular & Behavioral Neuroscience Institute.

Dr. Akil has made seminal contributions to the understanding of the neurobiology of emotions, including pain, anxiety, depression and substance abuse. She and her colleagues provided the first physiological evidence for a role of endorphins in the brain; and showed that endorphins are activated by stress and cause pain inhibition, a phenomenon they termed Stress-Induced Analgesia. Dr. Akil has investigated the molecular and neural mechanisms underlying stress reactivity and their relation to anxiety and depression, and is engaged in large scale studies to discover new genes and proteins that cause vulnerability to major depression and bipolar disorder. Dr. Akil's scientific contributions have been recognized with numerous honors and awards, including: the Pacesetter Award from the National Institute on Drug Abuse (NIDA), 1993; with Dr. Stanley Watson, the Pasarow Award for Neuroscience Research, 1994; the Sachar Award from Columbia University, 1998; and the Bristol Myers Squibb Unrestricted Research Funds Award, 1998. Dr. Akil is the past President of the American College of Neuropsychopharmacology (1998) and the past President of the Society for Neuroscience (2004). She was elected as a Fellow of the American Association for the Advancement of Science in 2000. In 1994, she was elected to the membership of the Institute of Medicine (IOM) of the National Academy of Science, and is currently a member of its Council. In 2004, she was elected to the American Academy of Arts and Sciences.



SARAH CADDICK, Ph.D.

Dr. Caddick is the Principal Advisor on Neuroscience to Lord Sainsbury of Turville and his charitable foundation, The Gatsby Charitable Trust. Formerly the Executive Director of the Center for Neuroscience

Initiatives at Columbia University Medical Center, she is a neuroscientist who has held leadership roles in private and public grant-making organizations where she has been responsible for the development, oversight and restructuring of strategic, programmatic, operational and grant-making activities. She had advised a number of individuals and Foundations on their philanthropy in science and has sat on various funding committees in the US. She is currently serves on the New York Academy of Sciences UK Charitable Foundation Board of Governors. Before pursuing a career in medical and scientific grant-making and policy, Dr. Caddick was engaged in biomedical research in epilepsy at Duke University Medical Center and the Medical College of Virginia. She holds a Ph.D. in neuroscience from the University of Southampton, U.K., and a B.Sc. in biology (Honors in neuroscience and genetics) from the University of Portsmouth, U.K.



H. CHRISTIAN FIBIGER, Ph.D.

Based in Barbados, Dr. Fibiger is Chief Scientific Officer of Biovail Laboratories International SRL.

His previous experience includes Vice President and Global Head of Neuroscience at Amgen (2003-07), and Vice President of Neuroscience Discovery Research and Clinical Investigation, and LRL Europe at Eli Lilly and Company (1998-2003). Prior to that, Dr. Fibiger served as Professor and Head of the Division of Neurological Sciences and Chair of the University Graduate Program in Neuroscience at the University of British Columbia in Vancouver. He has received many honors for his contributions to neuroscience research, including the Clark Institute Prize in Psychiatry, the Heinz Lehmann Award of the Canadian College of Neuropsychopharmacology, the Killam Research Prize, the Gold Medal in Health Sciences from the Science Council of British Columbia and the Tanenbaum Distinguished Scientist Award in Schizophrenia Research. Dr. Fibiger serves on the editorial boards of ten journals in the field of neuroscience, has been coeditor of *Neuropsychopharmacology*, and has authored or coauthored more than 400 scientific papers focused mainly on the neurobiological substrates of Alzheimer's disease, schizophrenia, depression and drug abuse. Dr. Fibiger has also served on a number of national and international scientific advisory boards including the National Institute of Mental Health (USA), the Canadian Psychiatric Research Foundation (Canada), the Medical Research Council (Canada), the Human Frontiers Science Program (International), and the National Alliance for Research on Schizophrenia and Affective Disorders (USA). Dr. Fibiger is a Fellow of the American College of Neuropsychopharmacology (ACNP). He received his B.Sc. in Chemistry and Psychology from the University of Victoria in 1966, and his Ph.D. in Psychopharmacology from Princeton University in 1970.



RUSSELL FOSTER, Ph.D.

Dr. Foster is Professor of Circadian Neuroscience and Head of the Nuffield Laboratory of Ophthalmology at the University of Oxford.

He gained his B.Sc. in Zoology (1980) and was awarded his Ph.D. (1984) from Bristol University. After post-doctoral studies in Bristol, Giessen, and Nijmegen, Dr. Foster moved to the USA in 1988 to become a member of the National Science Foundation Center for Biological Timing at the University of Virginia. He returned to the UK in 1995 to join the Department of Biology at Imperial College, and became Chair of the Department of Integrative and Molecular Neuroscience in 2000. In June 2006, he and his group moved to the University of Oxford where Dr. Foster was made HoD in May 2007. Dr. Foster chairs and participates in multiple committees for RCUK. He is a member of the strategy board for BBSRC, a member of the UK Panel for Research Integrity in Health and Biomedical Sciences, and a Faculty member of the Lundbeck Institute of Neuroscience in Denmark. In recognition of his research achievements he has been awarded the Honma prize (Japan), Cogan Award (USA), the Zoological Society Scientific Medal (UK) and the Edrige-Green Medal (UK). He is a visiting Professor at the Universities of Imperial College, Surrey and Western Australia, and in May 2008 he was elected as a Fellow of the Royal Society. Dr. Foster is a strong proponent of the public awareness of science, and he is a frequent speaker at national and international conferences relating to both his research and areas of science policy. With Leon Kreitzman he has published 'Rhythms of Life', which provides an introduction to the biology and importance of circadian rhythms to the non-specialist reader. The sequel, 'Seasons of Life', will be published in June 2009.



MICHAEL E. GREENBERG, Ph.D.

Dr. Greenberg grew up in Brooklyn, New York, attended Wesleyan University in Connecticut and received his Ph.D. from Rockefeller University in 1982.

Following postdoctoral training with Dr. Edward Ziff at New York University Medical School, Dr. Greenberg moved to Harvard Medical School in 1986. He is currently the Nathan Marsh Pusey Professor of Neurobiology and Chair of the Department of Neurobiology at Harvard Medical School. Dr. Greenberg's research interests span a broad range of topics related to the development of the nervous system. His characterization of signalling networks that control brain development has provided new insight into how disruption of normal nervous system development leads to neurological disorders including mental retardation and autism. Dr. Greenberg has received a number of awards for his research. In 2003, he was elected to the American Academy of Arts and Sciences. He is the 2006 recipient of the A. Clifford Barger Award for Excellence in Mentoring-Harvard Medical School and the 3rd Annual Edward M. Scolnick Prize in Neuroscience. In 2008, he was elected to the National Academy of Science and received the J. Allyn Taylor International Prize in Medicine.



JOHN A. HARDY, Ph.D.

Dr. Hardy is Professor of Neuroscience, Institute of Neurology at University College London and Visiting Senior Scientist, Laboratory of Neurogenetics, NIA/NIH.

Born in Nelson, England, Dr. Hardy received his B.Sc. (Hons) degree from the University of Leeds, UK (1976) and his Ph.D. from Imperial College, London, UK where he studied glutamate and dopamine pharmacology. Dr. Hardy received his postdoctoral training at the MRC Neuropathogenesis Unit in Newcastle upon Tyne, UK and then further postdoctoral work at the Swedish Brain Bank in Umeå, Sweden where he started to work on Alzheimer's disease. In 1985, Dr. Hardy became Assistant Professor of Biochemistry at St. Mary's Hospital, Imperial College, London, where he initiated genetic studies of Alzheimer's disease. He was appointed Associate Professor in 1989 and then took the Pfeiffer Endowed Chair of Alzheimer's Research at the University of South Florida, in Tampa in 1992. In 1996 he moved to the Mayo Clinic in Jacksonville, Florida, as Consultant and Professor of Neuroscience, and he became Chair of Neuroscience in 2000. In 2001, Dr. Hardy established his laboratory at the National Institute on Aging where he continues to conduct research on both Alzheimer's and Parkinson's diseases. For his contributions to Alzheimer's research, Dr. Hardy has received the Peter Debye Prize, Allied Signal Prize, MetLife Prize, Potamkin Prize, and Kaul Prize. He is the author of 374 articles, and in 2001 was named Honorary Professor of Neuroscience at University College London.



MICHAEL HÄUSSER, Ph.D.

Dr. Häusser is Professor of Neuroscience at University College London (UCL) and a Senior Research Fellow of the Wellcome Trust. He received his Ph.D. from Oxford University under the supervision of Julian Jack. He subsequently worked with Bert Sakmann at the Max-Planck-Institute for Medical Research in Heidelberg and with Philippe Ascher at the Ecole Normale Supérieure in Paris. He

established his own laboratory at UCL in 1997 and became Professor of Neuroscience in 2001. His group is interested in understanding the cellular basis of neural computation in the mammalian brain using a combination of experimental and theoretical approaches, with a special focus on the role of dendrites.



MICHAEL HOWLETT

Mr. Howlett is the President and Chief Executive Officer of the Mental Health Commission of Canada.

Most recently, Mr. Howlett was President and CEO of the Canadian Diabetes Association (CDA). Under his direction, the CDA grew to be a financially sound and effective national organization, internationally recognized as the authority in diabetes research, education and advocacy. Mr. Howlett's professional career spans three decades, and he is recognized both as a successful business leader and champion of causes that defend those who cannot defend themselves. Mr. Howlett is distinguished as a results-oriented business and non-profit sector leader. He has worked extensively with government, the medical and research community, and business, and is very active with philanthropic and charitable organizations. As founding President of Portage, Ontario, Mr. Howlett now sits on its Board. Mr. Howlett has also served on the Boards of The Children's Aid Foundation, The Institute for the Prevention of Child Abuse, Meritus and United Way. He is the recipient of a number of awards that recognize his contributions. Mr. Howlett continues to hold positions on numerous corporate and non-profit boards.



ULMAN LINDENBERGER, Ph.D.

Dr. Lindenberger, scientific member of the Max Planck Society, is Director of the Center for Lifespan Psychology at the Max Planck Institute for Human Development, Berlin, and Honorary Professor of Psychology at the Free University Berlin, the Humboldt University Berlin, and Saarland University, Saarbrücken, Germany. He studied in Berkeley and Berlin, and received his

doctorate in psychology from the Free University of Berlin in 1990. His main research is the study of lifespan changes in learning and behavioural plasticity, with an emphasis on functional and etiological links between sensory and cognitive development, and on associative and strategic components of episodic memory. He is also interested in lifespan changes in brain-behaviour mappings, psychological principles of successful aging technologies, and the neuronal basis and developmental function of interpersonal action coordination. His research combines cognitive, psychometric, and neuroscience research, and makes use of multivariate and multi-level methods with a special emphasis on statistical, neurocomputational, and formal modelling techniques. Dr. Lindenberger's work is published regularly in leading scientific journals. He is a member of numerous scientific societies, including the Wilhelm Wundt Society as well as the Selection Committee of the Alexander-von-Humboldt research awards, Alexander-von-Humboldt Foundation, Germany. Other memberships include the American Psychological Association, the American Psychological Society, the Behavior Genetics Association, the Deutsche Gesellschaft für Psychologie, the Deutsche Gesellschaft für Gerontologie und Geriatrie, and the Gerontological Society of America.



RICHARD MAYEUX, M.D., M.S.

Dr. Mayeux is the Gertrude H. Sergievsky Professor of Neurology, Psychiatry and Epidemiology at Columbia University in New York City. He is currently the Director of the Gertrude H. Sergievsky Center, the Co-Director of the Taub Institute for Research on Alzheimer disease and the Aging Brain at Columbia University Medical Center. Dr. Mayeux has led a multidisciplinary, population-based

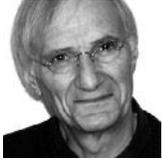
investigation of Alzheimer disease and other age-related disorders known as the Washington Heights-Inwood Community Aging Project. This study has provided the most current information on the rates of these diseases among elderly from African-American, Caribbean Hispanic and Whites, and uncovered the relationships between Alzheimer disease and environmental and medical risk factors, the genotypic variability of apolipoprotein- risk among different ethnic groups and the relationship of alterations in lipid metabolism and risk of dementia. More recently he was one of the lead scientists in a multi-national effort which ultimately identified genetic variants in the SORL1 as a putative genetic risk factor for Alzheimer's disease. He is current the national director of the National Institute on Aging Family Study of Alzheimer's Disease. Dr. Mayeux is the author of over 320 papers, chapters and books dealing with various aspects of degenerative diseases of the aging brain. He was elected to the Association of American Physicians, the American Epidemiological Society and The Institute of Medicine of the National Academy of Science. He has received many honors including: The Leadership and Excellence in Alzheimer disease Award from the National Institute of Aging for his investigation of genetic and environmental interaction in the etiology and pathogenesis of Alzheimer disease and related forms of dementia, and he was the recipient of the 2007 Potamkin Prize from the American Academy of Neurology. In 2008, Dr. Mayeux received the John Stearns Award for Lifetime Achievement in Medicine from the New York Academy of Medicine.



RÉMI QUIRION, O.C., Ph.D., F.R.S.C., C.Q.

Dr. Quirion is a McGill University Full Professor, Psychiatry (affiliation Neurology, Pharmacology and Therapeutics) and Scientific Director at the Douglas Mental Health University Institute.

Under his leadership, the Douglas Research Centre became a premier research facility in Canada in the fields of neurosciences and mental health. Dr Quirion promoted the development of neurosciences and clinical research in Neurology and Psychiatry as well as social and evaluation aspects of research in mental health and addiction. His research interests include: a) understanding the relationships between key phenotypes of the Alzheimer's brain and b) molecular and pharmacological features of neuropeptide receptors focusing on NPY and CGRP, and their role in memory, pain and drug dependence, and in animal models of schizophrenia. In addition to being on the Advisory Board of over 15 scientific journals in Psychiatry, Pharmacology, and Neurosciences, Dr. Quirion has published 5 books and more than 650 scientific papers and articles. Dr. Quirion is also the inaugural Scientific Director of the Institute of Neurosciences, Mental Health and Addiction. In addition to being one of the *most highly cited neuroscientists in the world*, Dr. Quirion received in 2003 the *Médaille de l'Assemblée nationale du Québec* and the "2003 First Annual Award — *National Mental Health Champion (Research)*". During the same year he also became a *Fellow of the Royal Society of Canada*, and a "Chevalier" of the "*Ordre national du Québec*". In 2004 he received the "*Wilder-Penfield Award, Prix du Québec*", the highest distinction in Biomedical Research in Quebec, and the *Dr. Mary V. Seeman Award* from the Canadian Psychiatric Research Foundation. He has been appointed *Fellow of the Canadian Academy of Health Sciences* in 2005. In 2007, Dr. Quirion became a *Member of the Order of Canada (O.C.)* and received the Schizophrenia Society of Canada's 2007 *Pacesetter Award*; the *Canadian College of Neuropharmacology 2007 Medal*, and the *Prix Michel Sarrazin*, of the Club de recherches cliniques du Québec.



MARTIN RAFF, M.D.

Dr. Raff was born and educated in Montreal. He received his B.Sc. and M.D. degrees at McGill University and did a residency in medicine at the Royal Victoria Hospital in Montreal and in neurology at the Massachusetts General Hospital in Boston. He did postdoctoral training in immunology at the

National Institute for Medical Research in London, after which he moved to University College London, where he has been a Professor of Biology since 1979 and emeritus from 2002. Dr. Raff is currently at the Medical Research Council Laboratory for Molecular Cell Biology at University College London. His research was in immunology, cell biology, and developmental neurobiology. He is a Fellow of the Royal Society, the British Academy of Medical Sciences, and the Academia Europaea, a Foreign Honorary Member of the American Academy of Arts and Sciences, and a Foreign Associate of the National Academy of Sciences. He was president of the British Society of Cell Biology from 1991 to 1995 and was chairman of the UK Life Sciences Committee from 1998-2001. Dr. Raff is a co-author of two widely used cell biology textbooks and is on many scientific advisory boards in Europe and America.



MARCUS E. RAICHLE, M.D.

Dr. Raichle, a neurologist, is a Professor of Radiology, Neurology, Neurobiology and Biomedical Engineering at Washington University in St Louis. He is a member of the National Academy of

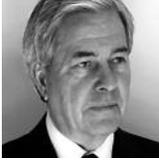
Sciences, The Institute of Medicine and the American Academy of Arts and Sciences and a Fellow of the American Association for the Advancement of Science. He and his colleagues have made outstanding contributions to the study of human brain function through the development and use of positron emission tomography and functional magnetic resonance imaging. Their landmark study (*Nature*, 1988) described the first integrated strategy for the design, execution and interpretation of functional brain images. Another seminal study led to the discovery that blood flow and glucose utilization change more than oxygen consumption in the active brain (*Science*, 1988) causing tissue oxygen to vary with brain activity. This discovery provided the physiological basis for subsequent development fMRI and caused researchers to reconsider the dogma that brain uses oxidative phosphorylation exclusively to fuel its functional activities. Finally seeking to explain task-induced activity decreases in functional brain images they employed an innovative strategy to define a physiological baseline (*PNAS*, 2001; *Nature Reviews Neuroscience*, 2001). This has led to the concept of a default mode of brain function and invigorated studies of intrinsic functional activity, an issue largely dormant for more than a century. An important facet of this work was the discovery of a unique fronto-parietal network in the brain that has come to be known as the *default mode network (DMN)*. This network is now the focus of work on brain function in health and disease worldwide. In summary, the Raichle group has consistently led in defining the frontiers of cognitive neuroscience through the development and use of functional brain imaging techniques.



TERRENCE J. SEJNOWSKI, Ph.D.

Dr. Sejnowski, professor and head of the Computational Neurobiology Laboratory, Salk Institute for Biological Studies, is a pioneer in the field of computational neuroscience. Dr. Sejnowski is

interested in the hippocampus, believed to play a major role in learning and memory; and the cerebral cortex, which holds our knowledge of the world and how to interact with it. In his lab, Sejnowski's team uses sophisticated electrical and chemical monitoring techniques to measure changes that occur in the connections among nerve cells in the hippocampus during a simple form of learning. They use the results of these studies to instruct large-scale computers to mimic how these nerve cells work. By studying how the resulting computer simulations can perform operations that resemble the activities of the hippocampus, Sejnowski hopes to gain new knowledge of how the human brain is capable of learning and storing memories. This knowledge ultimately may provide critical clues to combating Alzheimer's disease and other disorders that rob people of the critical ability to remember faces, names, places and events. Dr. Sejnowski received his B.S. in physics from Case Western Reserve University and his Ph.D. in physics from Princeton University. He received his postdoctoral training in biology at Princeton and in neurobiology at Harvard Medical School. He is the recipient of numerous awards and honors for his work including the Presidential Young Investigator Award, 1984-89; Fairchild Distinguished Scholar, 1992-93; Wright Prize, 1996; Hebb Prize, 1999; IEEE Fellow, 2000; Neural Network Pioneer Award, 2002; Johns Hopkins Society of Scholars, 2003; Francis Crick Chair funded by the J.W. Kieckhefer Foundation, 2004; and American Association Advancement of Science Fellow, 2006.



BRYCE WEIR, O.C., M.D.C.M., F.R.C.S.C., F.A.C.S., F.R.C.S.Ed (Hon)

Dr. Weir is the Goldblatt Professor Emeritus of Surgery and Neurology, former Director of the Brain Research Institute, Interim Dean of the Biological Sciences and Pritzker School of Medicine and Vice-President for Medical Affairs, all at The University of Chicago. He was awarded the Grass Gold

Medal of the Society of Neurological Surgeons and was elected to the Institute of Medicine of the National Academy of Sciences (USA). He is also the Anderson Professor Emeritus of Surgery and former Chairman of the Department of Surgery at the University of Alberta. In addition to many research reports, Dr. Weir has authored three textbooks and co-edited two others in the field of aneurysms and stroke. Dr. Weir has served as President of the Alberta Medical Association and the Canadian Congress of Neurological Sciences. Dr. Weir was the inaugural recipient of the Lifetime Achievement Award of the Canadian Society of Neurological Surgeons and is an Officer of the Order of Canada.



SAMUEL WEISS, Ph.D.

Dr. Weiss is Professor and Alberta Heritage Foundation for Medical Research (AHFMR) Scientist in the Departments of Cell Biology & Anatomy and Pharmacology & Therapeutics at the University of Calgary, Faculty of Medicine, and he is the inaugural Director of the Hotchkiss Brain Institute.

Dr. Weiss received his B.Sc. in Biochemistry at McGill University in 1978 and completed his Ph.D. in Chemistry (Specialization: Neurobiology) at the University of Calgary in 1983. Following post doctoral fellowships, funded by AHFMR and the Medical Research Council of Canada, at the Centre de Pharmacologie-Endocrinologie, Montpellier, France, and at the University of Vermont College of Medicine, Burlington, Vermont, Dr. Weiss was appointed Assistant Professor and MRC Scholar at The University of Calgary in 1988. Two major discoveries are the hallmarks of Dr. Weiss' research career. In 1985, together with Dr. Fritz Sladeczek, Dr. Weiss discovered the metabotropic glutamate receptor — now a major target for pharmaceutical research and development for neurological disease therapies. In 1992, Dr. Weiss discovered neural stem cells in the brains of adult mammals. This research has led to new approaches for brain cell replacement and repair. Dr. Weiss sits on numerous national and international peer review committees, has authored many publications, holds key patents in the neural stem cell field and has founded two biotechnology companies. In 2002, Dr. Weiss was awarded the Fondation IPSEN (France) prize in Neuronal Plasticity, in 2004 he received the Canadian Federation of Biological Societies Presidents' Award in Life Sciences Research, and in 2008 he was named recipient of a Gairdner International Award "for his seminal discovery of adult neural stem cells in the mammalian brain and its importance in nerve cell regeneration".

APPENDIX 2: EXPERTS CONSULTED

INTERNATIONAL CONSULTATIONS

UNITED STATES

LANDIS, STORY	Director, National Institute of Neurological Diseases and Stroke
INSEL, THOMAS R.	Director, National Institute for Mental Health (NIMH)
BARR, ROBIN	Director, Extramural Activities, National Institute of Aging (NIA)
MORRISON-BOGORAD, MARCELLE	Associate Director, National Institute on Aging's Neuroscience and Neuropsychology of Aging Program.

Harvard University

SANES, JOSH	Director, Center for Brain Science & Professor of Molecular and Cellular Biology, Harvard University
WALSH, CHRIS	Neurologist and Neurogeneticist supported by the Howard Hughes Medical Institute, Harvard University – Center for Brain Science
HENSCH, TAKAO	Developmental Neuroscientist, Harvard University – Center for Brain Science
RAVIOLA, ELIO	Bullard Professor of Neurobiology, Department of Neurobiology, Harvard Medical School

UNITED KINGDOM

CADDICK, SARAH	Principal Advisor, The Gatsby Charitable Foundation Cognitive Neuroscience
HARDY, JOHN	Chair of Molecular Biology, Neurological Disease at the UCL Institute of Neurology
BELL, SIR JOHN	President, Academy of Medical Sciences University of Oxford, Founder of the Wellcome Trust Centre for Human Genetics
FOSTER, RUSSELL	Chair of Circadian Neuroscience, University of Oxford
TRACEY, IRENE	Director, Oxford Centre for Functional Magnetic Resonance Imaging of the Brain (fMRI), Nuffield Professor of Anesthetic Science, and a Fellow of Medicine at Pembroke College
FLINT, JONATHAN	Wellcome Trust Principal Research Fellow, Michael Davys Professor, Consultant Psychiatrist, University of Oxford
DAYAN, PETER	Professor, Gatsby Computation Neuroscience Unit, University College London
DUZEL, EMRAH	Professor, Institute of Cognitive Neuroscience, University College London
BURGESS, PAUL	Institute of Cognitive Neuroscience & Dept. Psychology, University College London
BORYSIEWICZ, LESCEK	Chief Executive of the United Kingdom's Medical Research Council
DUNCAN, JOHN	Professor, MRC Cognition and Brain Sciences Unit, University of Cambridge
PULVERMULLER, FRIEDEMANN	MRC Programme Leader in the Cognitive Neuroscience of Language, Professor at the University of Wales, Anglia Ruskin University and St. Petersburg State University
CALDER, ANDY	MRC Cognition and Brain Sciences Unit, University of Cambridge
NORRIS, DENIS	MRC Cognition and Brain Sciences Unit, University of Cambridge
BARNARD, PHIL	MRC Cognition and Brain Sciences Unit, University of Cambridge
MARSLÉN-WILSON, WILLIAM	Director, MRC Cognitive Brain Unit, University of Cambridge
TYLER, LORRAINE	Professor, Department of Psychology, University of Cambridge
PATTERSON, ROY	Professor, Department of Psychology, University of Cambridge
PATTERSON, KARALYN	MRC Cognition and Brain Sciences Unit, University of Cambridge
WILLIAMS, JOHN	Director, Clinical Services, Wellcome Trust

MORRIS, RICHARD	Director, Neuroscience Programs, Wellcome Trust
MAGUIRE, ELEANOR	Professor, Wellcome Trust Centre for Neuroimaging
OTTEN, LEUN	Professor, Institute of Cognitive Neuroscience & Dept. Psychology, University College London
DRIVER, JONATHAN	Director, Institute of Cognitive Neuroscience & Dept. Psychology
CADWALLADER, GRAHAM	Neuroscience Strategy Coordinator, University College London
HÄUSSER, MICHAEL	Professor of Neuroscience, University College London

GERMANY

SINGER, WOLF	Director, Department of Neurophysiology, Founding Director of the Ernst Strüngmann Institute (ESI) Max Planck Institute (MPI)
UHLHAAS, PETER	Group Leader, Max Planck Institute
KAYSER, CHRISTOPHE	Scientist, Logothetis Lab, MPI, Tuebingen
MUNK, MATTHIAS	Scientist, Logothetis Lab, MPI, Tuebingen
BULTHOFF, HEINRICH	Director, Biological Cybernetics, MPI
STEIGER, AXEL	Senior Scientist, MPI for Psychiatry, Munich
BINDER, ELISABETH	Research group leader at the Max-Planck Institute of Psychiatry, Munich
MULLER, MARIANNE	Clinical Psychiatrist, MPI,
WEBER, MATHIAS	Assistant Director, MPI
REIN, THEO	Research Group Leader, MPI of Psychiatry
EDER, MATHIAS	Research Group Leader, MPI of Psychiatry
REFOJO, N.G.	Independent Junior Research Group Leaders, MPI
GASSER, THOMAS	Director, Neurodegeneration Group, Hertie Institute, Tuebingen
JUCKER, MATHIAS	Director, Cellular Neurology Group, Hertie Institute, Tuebingen
SCHOLS, LUDGER	Senior Scientist, Hertie Institute, University of Tuebingen
KAHLE, PHILIPP	Senior Scientist, Hertie Institute, University of Tuebingen
MELMS, ARTHUR	Senior Scientist, Hertie Institute, University of Tuebingen
DI GIOVANNI, SIMONE	Senior Scientist, Hertie Institute, University of Tuebingen

ONTARIO CONSULTATIONS

Ontario Cellular and Molecular Scientists

ALBERT, PAUL	Senior Scientist, Neuroscience, Ottawa Hospital Research Institute
BOULIANNE, GABRIELLE	Senior Scientist, Program in Developmental Biology, Hospital for Sick Children
CORDES, SABINE	Senior Investigator, The Samuel Lunenfeld Research Institute of Mount Sinai Hospital
CREGAN, SEAN	Scientist, Cell Biology, Robarts Research Institute, Assistant Professor, Physiology and Pharmacology, University of Western Ontario
CULOTTI, JOE	Investigator, Samuel Lunenfeld Research Institute
DIRKS, PETER	Scientist, Principal Investigator, Hospital for Sick Children and Associate Professor, Department of Surgery, University of Toronto

ELLIS, JAMES	Scientific Co-Director, Ontario Human IPS Cell Facility and Senior Scientist, Developmental and Stem Cell Biology, Hospital for Sick Children
HAKIM, TONY	Professor and University Chair, Neurology, University of Ottawa; Director, Neuroscience Research, Ottawa Health Research Institute; CEO and Scientific Director, Canadian Stroke Network; Scientific Director, Heart and Stroke Foundation of Ontario Centre for Stroke Recovery
JASMIN, BERNARD	Professor and Chair, Faculty of Medicine, University of Ottawa
JOSELYN, SHEENA	Scientist, Neurosciences & Mental Health, Assistant Professor, Department of Physiology, Hospital for Sick Children, Canada Research Chair, Molecular and Cellular Cognition
KISH, STEPHEN	Senior Scientist and Head of Human Neurochemical Pathology Laboratory, Centre for Addiction and Mental Health
MACKENZIE, ALEX	Chief Executive Officer and Scientific Director, Children's Hospital of Eastern Ontario Research Institute
POULTER, MICHAEL	Professor, Department of Physiology & Pharmacology, University of Western Ontario / Robarts Research Institute
SALTER, MICHAEL	Head & Senior Scientist, Neurosciences and Mental Health, Canada Research Chair in Neuroplasticity and Pain, Hospital for Sick Children, Professor of Physiology, University of Toronto
ST. GEORGE-HYSLOP, PETER	Professor in the Department of Medicine, Division of Neurology, and Director, Centre for Research in Neurodegenerative Disease, University of Toronto, Fellow of the Royal Society of Canada, elected as a foreign member to the Institute of Medicine of the National Academies
STRONG, MICHAEL	Director London Motor Neuron Diseases Clinic, London Health Sciences Centre, Arthur J. Hudson Chair in ALS Research, Scientist, Robarts Research Institute, Chief of Neurology and Co-chair Department of Clinical Neurological Sciences, London Health Sciences Centre and the University of Western Ontario
THOMPSON, JOHN	Full Adjunct Professor, Cross Appointed [Chemistry], Associate Vice President, University Research, University of Waterloo
ZHUO, MIN	EJLB-CIHR Michael Smith Chair in Neurosciences and Mental Health, Professor of Physiology, University of Toronto

Ontario Systems and Behavioural Scientists

BENINGER, RICK	Professor of Psychology & Professor of Psychiatry and member of the Centre for Neuroscience Studies, Queen's University
BLACK, SANDRA	Professor, University of Toronto, Dept of Medicine (Neurology), Neuroscience Program Research Director, Sunnybrook Research Institute
CRAWFORD, DOUG	Canada Research Chair in Visuomotor Neuroscience, CIHR Group for Action and Perception, York University
ELIASMITH, CHRIS	Associate Professor, Departments of Philosophy and Systems Design Engineering, The Centre for Theoretical Neuroscience, University of Waterloo
FEHLINGS, MIKE	Professor in the Department of Surgery, full member of the Institute of Medical Sciences School of Graduate Studies, Director of the Spinal Program at the Toronto Western Hospital, Director of the Neural and Sensory Sciences Program at the University Health Network and Krembil Chair in Neural Repair and Regeneration

GOLDBLOOM, DAVID	Senior Medical Advisor, Education and Public Affairs, at the Centre for Addiction and Mental Health, Professor of Psychiatry at the University of Toronto, Board Member and Vice Chair Mental Health Commission of Canada
GOODALE, MEL	Canada Research Chair in Visual Neuroscience in the Departments of Psychology and Physiology, University of Western Ontario
GRIMES, DAVID	Associate Scientist, Neuroscience, Ottawa Hospital Research Institute, Associate Professor, Division of Neurology, Department of Medicine, University of Ottawa, Director, Parkinson's Disease and Movement Disorders Clinic at The Ottawa Hospital, Co-Director of the Parkinson Research Consortium, Ottawa Health Research Institute
HENKELMAN, MARK	Professor in the Departments of Medical Biophysics and Medical Imaging at the University of Toronto, Director of the Mouse Imaging Centre (MICe) at the Hospital for Sick Children
LANG, TONY	Senior Scientist, Division of Patient Based Clinical Research, Morton and Gloria Shulman Movement Disorders Centre, Toronto Western Hospital, Division of Neurology, University of Toronto
MALER, LEN	Professor in the Department of Cellular and Molecular Medicine of the Faculty of Medicine, University of Ottawa
MCINTOSH, RANDY	Senior Scientist & Director of Rotman Research Institute of Baycrest Centre, Professor Department of Psychology, University of Toronto
MOSCOVITCH, MORRIS	Max and Gianna Glassman Chair in Neuropsychology and Aging, Professor, Department of Psychology, University of Toronto & Senior Scientist, Rotman Research Institute of Baycrest
MULSANT, BENOIT	Physician-in-Chief, Clinical Director, Geriatric Mental Health Program, Centre for Addiction and Mental Health, Professor, University of Toronto
MUNOZ, DOUG	Canada Research Chair in Neuroscience, Director, Centre for Neuroscience Studies, Professor of Physiology and Psychology, Member, CIHR Group in Sensory-Motor Systems, Queen's University
SEKULAR, ALLISON	Associate Vice-President & Dean of Graduate Studies, Canada Research Chair in Cognitive Neuroscience, Professor of Psychology, Neuroscience & Behaviour, Associate Member, The Brain-Body Institute, McMaster University & Adjunct Member, Centre for Vision Research, York University
THAGARD, PAUL	Professor of Philosophy, with cross appointment to Psychology and Computer Science, Director of the Cognitive Science Program, and University Research Chair at the University of Waterloo
TSOTSOS, JOHN	Distinguished Research Professor, Canadian Research Chair in Computational Vision, Department of Computer Science and Engineering, York University
VACCARINO, FRANCO	Principal, University of Toronto Scarborough
WILSON, HUGH	ORDCF Professor of Vision Research, Department of Biology, York University

Ontario Medical Devices and Technology Scientists

CHEN, ROBERT	Senior Scientist, University Health Network, Toronto Western Hospital, Associate Professor, University of Toronto
FERNIE, GEOFF	Vice President, Research at Toronto Rehabilitation Institute, Professor in the Department of Surgery at the University of Toronto & cross-appointments with the Institute of Biomaterials and Biomedical Engineering, the Graduate Department of Rehabilitation Science and the Departments of Mechanical and Industrial Engineering, Physical Therapy and Occupational Therapy

GRAHAM, SIMON	Associate Professor, Department of Medical Biophysics, University of Toronto, Rotman Research Institute of Baycrest Centre
GUENTHER, AXEL	Senior Scientist, Section Head and Group Leader, Department of Mechanical and Industrial Engineering, University of Toronto, Institute of Biomaterials and Biomedical Engineering
JAFFRAY, DAVID	Head, Radiation Physics, Associate Professor, Division of Biophysics and Bioimaging, Ontario Cancer Institute, University Health Network, Princess Margaret Hospital
LOZANO, ANDRES	Professor in the Department of Surgery, and inaugural Chair Holder of the Ron Tasker Chair in Stereotactic and Functional Neurosurgery at the University Health Network, Canada Research Chair in Neuroscience, Division of Brain Imaging & Behaviour Systems – Neuroscience, Toronto Western Hospital
MENON, RAVI	Canada Research Chair in Functional and Molecular Imaging at the Robarts Research Institute and Professor of Medical Biophysics, Diagnostic Radiology & Nuclear Medicine, Physics and Psychiatry at the University of Western Ontario
MERALI, ZUL	President/CEO of the University of Ottawa Institute of Mental Health Research (IMHR) and full professor in the faculties of Medicine (Departments of Cellular and Molecular Medicine and Psychiatry) and Social Sciences (Psychology) at the University of Ottawa, and research professor at the Institute of Neuroscience at Carleton University
POPOVIC, MILOS	Toronto Rehabilitation Institute Chair in Spinal Cord Injury Research, and Assistant Professor in the Institute of Biomaterials and Biomedical Engineering at the University of Toronto
SCOTT, STEPHEN	Professor, Queen’s University Department of Anatomy and Cell Biology, Centre for Neuroscience Studies
STROTHER, STEPHEN	Senior Scientist, Rotman Research Institute of Baycrest Centre, Professor Department of Medical Biophysics, University of Toronto

Ontario Clinicians

FISMAN, SANDRA	Chair, Psychiatry, Schulich School of Medicine & Dentistry, University of Western Ontario & Chief, Psychiatry, UWO Affiliated Hospitals
GILLIS, KATHARINE	Chair, Department of Psychiatry, University of Ottawa
RUTKA, JAMES	Co-director of the Labatt Brain Tumor Research Centre, and Chair, Division of Neurosurgery, University of Toronto
POKRUPA, RONALD	Department of Surgery, Chair, Division of Neurosurgery, Queen’s University, Neurosurgeon at the Kingston General and Hotel Dieu Hospitals
WILLIAMSON, PETER	Chair, Division of Neuropsychiatry, University of Western Ontario

Ontario Brain Surgeons

LOZANO, ANDRES	Professor in the Department of Surgery, and inaugural Chair Holder of the Ron Tasker Chair in Stereotactic and Functional Neurosurgery at the University Health Network, Canada Research Chair in Neuroscience, Division of Brain Imaging & Behaviour Systems – Neuroscience, Toronto Western Hospital
MACDONALD, LOCH	St. Michael’s Hospital Head, Division of Neurosurgery and the first Keenan endowed chair and Professor of Surgery, University of Toronto, Department of Surgery, Division of Neurosurgery

POKRUPA, RONALD	Department of Surgery, Chair, Division of Neurosurgery, Queen's University, Neurosurgeon at the Kingston General and Hotel Dieu Hospitals
RAICHLE, MARCUS	Professor of Radiology, Neurology, Neurobiology and Biomedical Engineering at Washington University in St Louis
RUTKA, JAMES	Co-director of the Labatt Brain Tumor Research Centre, and Chair, Division of Neurosurgery, University of Toronto
STRAFELLA, ANTONIO	Senior Scientist, Division of Brain Imaging & Behaviour Systems – Neuroscience, Toronto Western Research Institute
TATOR, CHARLES	Professor, Department of Surgery, Division of Neurosurgery, University of Toronto
WEIR, BRYCE	Chief of Neurosurgery and Director, University of Chicago – Emeritus

Ontario Industry Leaders

ANSEL, CLIFF	President, Thornhill Research
COULL, JEFFREY	President, GM, Chlorion Pharma
DREISMANN, HEINER	Director, GeneNews
FIBIGER, CHRIS	Senior Vice President, CSO, Biovail Corporation
GIOVINAZZO, TONY	CEO, Cervelo Pharmaceuticals Ltd
LAVERTU, GENEVIEVE	Director, Legal Affairs and Business Development, Medtronics
SELA, GAL	Founder, Chief Technology Officer, Sentinelle Medical Inc
UNDERDOWN, BRIAN	Managing Director, Lumira Capital
XANTHOUDAKIS, STEVEN	Director, Licensing and External Research, Merk Frosst Canada

Other Ontario Consultations

GARFINKEL, PAUL	President and CEO of Centre for Addiction and Mental Health (CAMH)
HUDSON, TOM	President and Scientific Director, Ontario Institute for Cancer Research, Professor, Department of Medical Genetics and Microbiology, and Department of Medical Biophysics, University of Toronto, Vice-Chair, Board of Directors, Genome Canada
SHOICHET, MOLLY	Professor, Department of Chemical Engineering and Applied Chemistry, Department of Chemistry, Terrence Donnelly Centre for Cellular and Biomolecular Research, and Institute of Biomaterials and Biomedical Engineering and Canada Research Chair in Tissue Engineering, University of Toronto. Member of Canada's Science Technology and Innovation Council
STUSS, DONALD	Rotman Research Institute of Baycrest Centre, Reva James Leeds Chair in Neuroscience and Research Leadership & University Professor, Department of Psychology, Faculty of Arts and Science; Department of Medicine (Neurology), Faculty of Medicine; Centre for Studies of Aging, University of Toronto

APPENDIX 3: WORKING GROUP

JOSEPH B. MARTIN, M.D., Ph.D.

Dr. Martin is a co-founder and co-chair of the Harvard NeuroDiscovery Center. He is the Edward R. and Anne G. Lefler Professor of Neurobiology and the former Dean of the Faculty of Medicine, Harvard Medical School (1997-2007). Born in Bassano, Alberta, Dr. Martin received his early medical education at the University of Alberta in Edmonton. He earned his Ph.D. from the University of Rochester in 1971, and began his career in academic medicine at McGill University, where he became chair of the Department of Neurology and Neurosurgery in 1977. In 1978, Dr. Martin joined the faculty of Harvard Medical School as the Bullard Professor of Neurology and chief of the Neurology Service at Massachusetts General Hospital. In 1984, he was appointed the Julieanne Dorn Professor of Neurology at Harvard. Dr. Martin served as Dean of the School of Medicine at the University of California, San Francisco (UCSF) from 1989 to 1993, and was elected Chancellor of UCSF for four years until returning to Harvard. Dr. Martin's numerous contributions have included the fostering of new health service models that significantly enhance research and improve access to quality care. In 2006 Dr. Martin was named the inaugural winner of The Henry G. Friesen International Prize in Health Research.

JOSEPH L. ROTMAN, O.C., LL.D.

Mr. Rotman is Chairman of Roy-L Capital Corporation, which is a private family investment company. He launched his business career in 1962 and has been involved in establishing a number of private and public companies in many different industries. Mr. Rotman has applied his business experience to the advancement of Canadian life sciences research, the development of Canada's innovation and commercialization capacity, and related public policy at the federal and provincial levels. He led the creation of the Rotman Research Institute at Baycrest Centre for Geriatric Care affiliated with the University of Toronto, and served two three-year terms on the Governing Council of the Canadian Institutes of Health Research (CIHR) from June 2000 to June 2006. He has served as a Director on numerous corporate boards including the Bank of Montreal, Barrick Gold Corporation, Canada Northwest Energy Ltd., Masonite International, and TrizecHahn Corp. He also served as Chair of the Board as Founder of Tarragon Oil and Gas, Geocrude Energy, and PanCana Resources, amongst others. As the Founder he remains a Director of Clairvest Group Inc., which provides merchant banking for emerging companies and is listed on the Toronto Stock Exchange. Mr. Rotman received his B.A. from the University of Western Ontario in 1957 and his M.Comm from the University of Toronto in 1960. During 1960-61, he studied at the Columbia University Graduate School of Business in the Ph.D. program. Mr. Rotman was awarded an honorary LL.D. from the University of Toronto in 1994. In 1995, he was made an Officer of the Order of Canada, and in August 2008 Mr. Rotman was appointed Chair of the Canada Council for the Arts.

RICHARD A. MURPHY, Ph.D.

Dr. Murphy is the former Interim President of the California Institute of Regenerative Medicine (California's Stem Cell Institute) and immediate Past President and CEO of the Salk Institute for Biological Studies in La Jolla, CA. Born in Massachusetts, Dr. Murphy received his undergraduate degree from the College of Holy Cross in Worcester, MA in 1966, and a Ph.D. in zoology from Rutgers University in New Brunswick, NJ in 1974. After two years of postdoctoral research at Boston's Massachusetts General Hospital, Dr. Murphy was appointed assistant professor at Harvard Medical School's Department of Cell Biology and Anatomy, where he was funded by a Sloan Fellowship and a NIH Career Development Award. At Harvard he won numerous teaching awards and conducted an active research program in neurotrophins, proteins that promote the growth and survival of nerve cells and appear to play a role in memory and neurodegenerative diseases. Dr. Murphy left Harvard in 1986 to chair the Department of Anatomy and Cell Biology at the University of Alberta. While continuing his laboratory research, he restructured that department and amassed a record of achievement that led to his appointment in 1992 as director of the Montreal Neurological Institute, a teaching and research institute affiliated with McGill University, where he served for eight years.

FERGUS I.M. CRAIK, Ph.D., F.R.S.C.

Dr. Craik is Senior Scientist at the Rotman Research Institute and Professor Emeritus of Psychology at the University of Toronto. Born in Edinburgh, Scotland, Dr. Craik obtained his B.Sc. in Psychology at the University of Edinburgh in 1960 and obtained his Ph.D. from the University of Liverpool in 1965. His thesis work was on age related changes in confidence and decision making, and he also became interested in the effects of aging on memory and related cognitive processes. Dr. Craik was on the faculty of Birkbeck College, University of London from 1965 to 1971. In 1971 he joined the University of Toronto and was appointed University Professor of Psychology in 1997. He held the Glassman Chair of Neuropsychology from 1996 until his retirement from the university in 2000. He has been on many university committees, and chaired the Department of Psychology (1985-1990). Honours include Fellowships of the Canadian and American Psychological Associations; Killam Research Fellowship (1982-84); Fellow of the Royal Society of Canada (1985); the Killiam Prize for Science (2000); Fellow of the Royal Society of London (2008). Dr. Craik has been associated with the Rotman Research Institute at Baycrest since 1988, and was appointed Senior Scientist in 2000.

LOUIS SIMINOVITCH, Ph.D.

Dr. Siminovitch is Research Director Emeritus at the Samuel Lunenfeld Research Institute at Mount Sinai Hospital as well as University Professor Emeritus at the University of Toronto, where he was instrumental in establishing and developing the Department of Medical Genetics. He conducted research and provided leadership as founding Research Director at the Samuel Lunenfeld Research Institute after being geneticist-in-chief at the Hospital for Sick Children and earlier at the Ontario Cancer Institute, which he set up. Concurrently, he was on the faculty of the University of Toronto, which he joined after beginning his career at Connaught Medical Research Laboratories in Toronto. He has published nearly 150 research papers. He has been awarded Canada's Centennial Medal (1967), the Queen Elizabeth II Jubilee Silver Medal (1977), and companion's rank in the Order of Canada. He is a Fellow of the Royal Society of Canada and of the Royal Society (London), winner of the Gairdner Foundation Wightman Award and the Izaak Walton Killam Memorial Prize, an inductee in the Canadian Medical Hall of Fame, and a foreign associate of the National Academy of Sciences (US). He has also received several honorary degrees. He earned his bachelor's degree and PhD in Biochemistry from McGill University and completed a postdoctoral fellowship at the Institut Pasteur in Paris.

MARK J. POZNANSKY, C.M., O. Ont., B.Sc., Ph.D.

Dr. Poznansky is President, G2G Consulting, Toronto, Canada and Chairman of the Board of the Ontario Genomics Institute. A native of Montreal, Dr. Poznansky was educated at McGill University where he received his Ph.D. in Physiology in 1970. Dr. Poznansky completed his postdoctoral training in Biophysics at Harvard Medical School, where he held the position of Lecturer in Biophysics. In 1976, Dr. Poznansky returned to Canada as Associate Professor of Physiology at the University of Alberta in Edmonton. He rose to become the Associate Dean of Research at the university (1984-1993), where he was instrumental in the creation of several start-up biotechnology companies. In 1993, Dr. Poznansky moved to London, ON as President and Scientific Director of Robarts Research Institute where he oversaw the quadrupling of research activities and the establishment of several spin-off companies, including one that was sold to GE Healthcare. Dr. Poznansky is a founder of London Biotechnology Incubator Inc., and a founding member and past chair of the Council for Health Research in Canada, a research advocacy group in Ottawa. He also chaired the Scientific Advisory Board of the Canadian Medical Discoveries Fund, served on the Selection Committee, Canadian Network of Centres of Excellence and Medical Research Council of Canada Grants Panel, and is the holder of several patents. He serves on the boards of several biotechnology companies and numerous provincial and national research committees, and he is a senior advisor to the CEO of the newly created Thunder Bay Regional Research Institute. Dr. Poznansky continues to lecture widely, both nationally and internationally, in areas related to the Bio-Pharmaceutical Industry, research administration and funding.

BARBARA MILLER, B.Sc., M.B.A.

Ms. Miller is President and CEO of Woodwyld Inc. Her previous positions include Deputy Minister of the Ontario Ministry of Economic Development and Trade; Division President, Ault Foods/Parmalat; Chief Administrative Officer/Director, Food Industry Competitiveness, Ontario Ministry of Agriculture, Food and Rural Affairs; and Category Director (Marketing), with the Campbell Soup Company. Ms. Miller obtained her Bachelor of Food Science from the University of Guelph and a Masters in Business Administration from Queen's University. Ms. Miller is Chair of the Innovation Institute of Ontario, past Interim Chair of Agricorn, an agricultural risk management agency of the Ontario government, and a member of the Board of Governors for the University of Guelph.

MICHELE NOBLE, B.A.

Ms. Noble is President of Michele Noble and Associates Inc. Ms. Noble obtained her B.A. at the University of Western Ontario. She began her public service career with the federal government and then worked briefly in the private sector before joining the Ontario government. A Deputy Minister with the Ontario Government for ten years, Ms. Noble has extensive line department and central agency experience and was Secretary of Management Board of Cabinet from 1995 to 2001. Ms. Noble was also Deputy Solicitor General and Deputy Minister of Correctional Services, Deputy Minister of Revenue, and a member of the Canadian Comprehensive Auditing Foundation (CCAF) Task Force on Management Principles for Public Performance Reporting. Additionally, Ms. Noble was part of the four-member Cancer Initiative Working Group responsible for the analysis of the opportunities for a significant investment in cancer research in Ontario as well as managing the consultation and preparation of the subsequent Report to Government on the implementation plan for a new cancer institute.

KEITH PINDER, B.A.

Mr. Pinder is a consulting specialist with the Innovation Institute of Ontario (IIO), and Corporate Secretary to the Ontario Genomics Institute since his retirement from the Ontario government in 2000. During a 28 year career with the Ontario government, he held senior management positions in policy development and coordination, rural development, land use planning and insurance portfolios, in the Ministries of Finance, Municipal Affairs and Agriculture, Food and Rural Affairs. Mr. Pinder received his Bachelor of Arts from York University in 1970.

KATY NAU, B.A., M.A.

Ms. Nau is a consulting specialist with the Ontario Innovation Trust (OIT). Ms. Nau received her Bachelor of Arts in Mathematics and Psychology from the University of Adelaide, South Australia (1967) and Master of Arts in Psychology from the University of Toronto in 1969. Prior to her retirement in 2007, Ms. Nau was Manager, Secretariat for the Ontario Research and Innovation Council with the Ontario Ministry of Research and Innovation. Ms. Nau's previous positions include Coordinator, Institutional Relations, Canada Foundation for Innovation (1998-2005), Senior Policy Analyst, Health Canada (1997-98), and Senior Research Consultant, Ontario Ministry of Health and Long-Term Care (1990-97).

