As Provost of McGill University, I am pleased to present the Montreal Neurological Institute’s first CECR Annual Report detailing the activities and progress achieved over the course of the first year of support as is required by the Funding Agreement (Article VIII) between ourselves and the Government of Canada, in which the MNI is recognized as a Centre of Excellence in Commercialization and Research.

McGill is extremely proud of the MNI’s many accomplishments and we are honored to have received this prestigious award that recognizes the Institute’s contributions to a variety of fields in neuroscience and to advances in health care.

As you will read in the following pages, the CECR funding has allowed MNI faculty members and their colleagues to harness their ideas in a highly focused way and to advance in the discoveries and treatments that will benefit the health care of Canadians. The reports within reflect the innovations in research and clinical practise that are the hallmark of the MNI and confirm its global standing of excellence. Indeed, it is the tight link between bench research and bedside care that distinguishes the MNI’s now 75 years of quality as measured against the highest international standards.

I am confident that the success of the MNI in the first year of the CECR award will continue to contribute to an integrative scientific and clinical approach to understanding and treating neurological disorders.

Anthony C. Masi
Provost
McGill University
We have completed our first year of the CECR Award and a comprehensive report of our activities under its auspices is presented in the following pages. You will see that our CECR funding has produced many successes and we believe that our unique approach to using these funds will continue to prove highly successful.

The CECR funds could not have come at a better time for us. The Neuro, which is a fusion of the Montreal Neurological Institute and Hospital, is marking its 75th Anniversary this Fall, and we have much to celebrate.

The Neuro is at the forefront of research in neuroscience and state-of-the-art treatment of patients with neurological conditions. As such, we are constantly looking to develop new technologies and new operational systems to tackle the most pressing problems in neuroscience, neurology and neurosurgery. The CECR Award has allowed us to catapult our most interesting, high-risk programs to the forefront of our current efforts and to jumpstart programs that we would not have been able to otherwise. The CECR funding will have significant impact and this investment will have lasting value.

I am proud and delighted to present this first annual report to you. I thank Dr. Philip Barker and his Internal Review Committee for the time-consuming and thoughtful evaluation of each proposal that was submitted for funding under this Award. We at The Neuro are grateful for the support we have received over the years from the Governments of Canada and Quebec, from foundations, and from dedicated private citizens. All have contributed to the overwhelming success of The Neuro over these last 75 years.

David Colman, PhD
Director of the Neuro

Disorders of the nervous system are among the most serious health problems in developed societies, and account for more hospitalizations, long-term care, and chronic suffering than nearly all other medical conditions combined. Almost 50% of all Canadians, or 15 million people, will experience the devastation of a neurological disorder.

A teaching and research institute dedicated to advances in neuroscience

The Montreal Neurological Institute’s mission is as true today as it was in 1934 when it first opened its doors: to generate fundamental information about the nervous system and to apply that knowledge to understanding and treating neurological diseases. With 12 research units integrated with the clinical care activities of the Montreal Neurological Hospital, The Neuro, as the Institute and Hospital are known as, is recognized in the international community as an outstanding neuroscience research institute and tertiary care hospital and clinical facility. Our strengths include: molecular and cellular biology research programs in the Centre for Neuronal Survival and the Cell Biology of Excitable Tissues Group, Epilepsy Research and Treatment, Cognitive Neuroscience, Neuroimmunology, Complex Neural Systems, Neuromuscular Diseases and the McConnell Brain Imaging Centre.

As a teaching and research institute of McGill University, the MNI is the centerpiece not only of McGill’s strategic plan in the neurosciences but also of research and training in this field. The MNI maintains key collaborations with neuroscientists across the McGill network, as well as scientists in other universities and centers across Quebec and Canada, and around the world. About 50 faculty members lead international research teams that generate research and translational support from grants and contracts of approximately $27M per year. Close to 120 Masters and Doctoral students and 45 postdoctoral Fellows from around the world pursue their studies and scientific training at the MNI each year.

A centre for state-of-the-art treatment of neurological diseases

The founder of the MNI, Dr. Wilder Penfield, established a centre that integrates scientific activities and clinical care, an innovative approach in 1934 that has proved to be highly successful. Throughout its 75 year history and through its numerous accomplishments, the MNI has demonstrated its capacity to engage in the full spectrum of neuroscience research and to create an ideal environment for translational research. The close interaction among scientists and clinicians brings tangible results for patients afflicted with a neurological disorder: our Clinical Research Unit enables patients to participate in studies of the newest treatments for Parkinson’s, epilepsy, multiple sclerosis, migraine, or amyotrophic lateral sclerosis (ALS); researchers in the Brain Tumour Research Centre work closely with the Neurosurgical Research Group; and patients also benefit directly from the MNI’s technological resources and expertise in brain imaging, neuro-radiology, neuro-navigation and neuro-stimulation.

A centre of excellence that positions Canada for global science leadership

The MNI’s goal is to provide an environment that allows neuroscientists and clinicians to identify the cellular basis of neurological disease and to translate these findings to innovations in clinical practise. We strongly believe that these innovations are best driven by the researchers and clinicians who are experts in their respective areas. The MNI’s status as a premier neuroscience institute attracts leading investigators, accomplished clinicians and promising students. Current MNI personnel come from more than 60 countries, and over 1350 former MNI trainees have established careers at universities and hospitals around the world. The numerous awards received by MNI investigators, our outstanding success rate in obtaining grants and the wealth of publications in leading scientific journals attest to our standing as a world-class institute with an extremely strong international reputation.

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The MNI was among the first seven recipients of the Centre of Excellence in Commercialization and Research Award issued by the Government of Canada in 2007. Traditional funding sources do not allow for development of dedicated, innovation-driven multidisciplinary research groups whose ideas and work can lead to potential new therapies. The CECR funding of $15M is allowing us to do this.

The MNI’s strategy for the CECR funding is consistent with the Federal government’s plan to help the research community translate ideas into innovations, provide solutions to health problems and create opportunities for increased economic productivity and competitiveness. Our overall strategy focuses on accelerating basic and translational research that will lead to rapid changes in healthcare delivery in neurology and neurosurgery. It also focuses on supporting innovations that will provide opportunities for commercialization of diagnostic or treatment measures. We will engage this strategy through the pursuit of five general objectives. In each of these objectives, we will use CECR funding towards salary support for specialized research personnel, and essential equipment maintenance contracts.

**Objective 1**

ACCELERATE NEW RESEARCH IN THE AREAS OF:

(a) biological basis of neurological disease
(b) neuroengineering
(c) translational neuroscience
(d) applied neuroscience and commercialization

In the area of the biological basis of neurological disease, our activities will focus on expanding our capacity for understanding the cellular basis of disease. This will allow for the development and analysis of genetic models to identify disease mechanisms and to define new therapies. The funds will also allow us to build dedicated research groups whose work will focus on the cell biology of neurological diseases and disorders such as brain tumours, motor neuron disease, multiple sclerosis, spinal cord regeneration and Parkinson’s disease. The Preclinical Assessment Unit that we will establish will serve to identify and develop promising therapies for these neurological disorders, thereby contributing directly to the development of, and interaction with translational neuroscience.

At the MNI, we have initiated a Neuroengineering Program that brings together nanotechnologists, chemists, physicists, computer scientists and engineers at McGill University. Their collaborative work aims to develop means by which the neuronal function can recover after disease or injury through interfaces between technological tools and the nervous system. In each of these endeavours, our aim is to ensure potential for commercialization and application to health care.

**Objective 2**

ENHANCE CLINICAL TRIALS PROGRAMS TO SUPPORT WORK IN TRANSLATIONAL NEUROSCIENCES

The MNI will achieve this objective by:

• expanding the Experimental Therapeutics Program, established in 2007 by Dr. Amit Bar-Or to assess the efficacy of new and established therapies. Funds will be used to provide analytical and statistical support to this program, which in turn will allow us to create new clinical research programs in brain tumours, Parkinson’s disease and stroke;

• developing its research on best practices in therapeutics and patient care. We aim to develop an investigator-initiated clinical trials program that will support clinical studies in therapeutics and spinal surgery techniques. We will also establish a new program that will support research to determine best practice in neuro-palliative care;

• developing web-based translational tools designed to bring research results and best practices to clinicians and other healthcare providers. These tools, consistent with the technological basis of communication today, will enable primary care physicians and practitioners to integrate new therapies and treatments into clinical care in a more timely fashion;

• establishing an international network for the Brain Imaging Centre. Joint international efforts aimed at understanding the structure and function of the normal brain and the mechanisms of specific brain disorders are accelerating. The MNI will build on its status as a world leader in techniques in brain imaging by providing resources to position the Brain Imaging Centre as the central hub of an emerging international network.

**Objective 3**

ENGAGE DOMESTIC AND INTERNATIONAL STUDENTS AND YOUNG RESEARCHERS IN OUR PROGRAMS

All of our projects will be structured to provide a learning and research environment for students and Fellows. In particular, MNI Fellows will be supported by CECR funds and will be deployed to the teams to achieve research goals and to facilitate commercialization of research results.

**Objective 4**

FACILITATE INTELLECTUAL PROPERTY PROTECTION, COMMERCIALIZATION OF RESEARCH RESULTS, AND BUSINESS DEVELOPMENT OF MNI INVENTIONS

Several initiatives and promising opportunities for commercialization exist at the MNI, including novel methods for enhancing spinal cord regeneration and for treatment of brain tumours. The MNI’s initiative in Applied Neuroscience and Commercialization will be managed with the support of a panel of business, financial and scientific consultants who have extensive experience in biotechnology and pharmaceutical industries. This panel will be convened on a regular basis and will advise the MNI on commercialization potential, methods and opportunities.

**Objective 5**

EXPAND PUBLIC OUTREACH AND ENGAGEMENT ACTIVITIES

The MNI will allocate funding to support three measures that will improve our national and international outreach:

• an International Student and Fellowship Program to provide much-needed stipends for trainees. This measure will enhance our ability to attract international students;

• a MNI conference series to be held annually and that will bring top tier international scientists to Montreal to present their latest work in areas of clinical importance and emerging research technologies. These conference series will help build scientific collaborations and facilitate the recruitment of the best research and clinical Fellows to the MNI;

• a portion of the CECR fund will be used to bolster our web resources and to develop new media for communicating our activities, research and results to the lay public.
Our Corporate Plan for the first year of the CECR award allowed us to structure our internal processes for management of CECR funded activities and to ensure allocation of the award according to the objectives defined in our global strategy.

Expected short term and medium term goals for 2008-2009

Our immediate goals for 2008-2009 were to establish the administrative and governance framework for identifying opportunities within the MNI with the greatest commercial and translational potential. Our governance structure would ensure that our overall strategy is sound and that activities related to CECR funding are carried out in a responsible manner. An Internal Review Committee would be constituted to evaluate proposals and allocate funding to high priority projects. As well, a Commercialization Committee would serve as an advisory body on all potential commercial activities and ensure that such projects are provided with the necessary tools for success. Lastly, a Centre of Excellence Advisory Board composed of leaders in academic and translational neuroscience and in biomedical commercialization would provide global oversight.

Performance metrics would be developed and introduced as web-based performance monitoring tools designed to link progress reports to disbursement of funds.

In our first year, we also expected: i) to identify projects and core activities for CECR funding; ii) initiate funding; iii) initiate intellectual property protection (patents and registration); iv) introduce and optimize web-based monitoring tools.

Our internal application process would focus on identifying and funding the best of our clinicians’ and researchers’ work, and it would ensure that applications are evaluated against criteria that are consistent with the goals of the Federal Science and Technology Strategy.

Planned expenditures for the first year were categorized as follows:

- Biological basis of neurological disease and neuroengineering (new basic research programs) $1,802,000
- Translational neuroscience $1,530,000
- Intellectual property protection, commercialization of research results and business development of MNI inventions $518,000
- Training aspects $760,000
- Public outreach and engagement activities $390,000

**TOTAL** $5,000,000

Actual funding per category and per project is presented in a later section.

In the first year of the CECR award...
The MNI attained the objectives that it set out in its Corporate Plan.

The MNI established:
- an Internal Review Committee to evaluate proposals and allocate funding
- a Commercialization Committee to advise on potential commercial activities
- a Centre of Excellence Advisory Committee to provide oversight

The MNI allocated close to $4M in funding to 36 new research activities in the biological basis of neurological disease, neuroengineering, translational neuroscience, clinical trials, and applied neuroscience and commercialization.

The MNI expanded its core facilities in translational health research.

The MNI awarded 10 Fellowships as part of its CECR Fellowship program for a total of $375,000.

The MNI allocated $370,000 to a number of public outreach and engagement activities.

The MNI developed web-based performance monitoring tools.

MNI Principal Investigators, as part of their CECR-funded activities:

- Engaged 15 Baccalaureate, Masters’ and Doctoral students and 9 post-doctoral Fellows
- Hired 43 research assistants and technicians and other qualified personnel
- Filed 5 patent applications
- Generated initial revenues of $60,000 from 2 commercial activities
- Confirmed industry collaborations with 3 companies in the pharmaceutical and biotechnology fields

FIRST YEAR RESULTS
In the first year of our CECR award, we received over 60 proposals for the three-year funding period, for a total of $50M in budget requests. Thirty-eight (38) of these were accepted by our Internal Review Committee for an initial 12 months’ funding which, for most projects, began between June and September 2008. The quarterly updates submitted by investigators enable us to measure progress against milestones for each funded project.

In the pages that follow, we provide more information on the work that was engaged in 2008-2009.
If It’s There, We’ll Find It

Roughly one-third of epilepsy patients suffer seizures that do not respond to drug treatments. Uncontrolled epilepsy has devastating socio-economic consequences, is harmful to the brain and is associated with higher mortality.

Surgery is the only effective treatment for these people. More than 90% of patients become free of seizures and enjoy greatly improved quality of life when the brain lesion is found and removed. Removing the lesion is seldom a problem, but finding it is.

Many times, the lesion is tiny and almost undetectable. Cortical Dysplasia, a malformation of brain cells that can start in the fetus, is present in 70% of severe cases of epilepsy but is very difficult to localize. As a result, the number of surgeries is much lower and the prognosis much poorer than for other lesions.

“It can be extremely hard to see on a scan,” says Dr. Andrea Bernasconi, who has been working on a solution for the past eight years. “There are many reasons why you might miss it, and so the patient never receives treatment.”

Led by Bernasconi, the Neuroimaging of Epilepsy Laboratory at the MNI has developed a unique set of tools that supply a solution. These are based on computer modeling that will automatically detect and delineate cortical dysplasia on an MRI scan and reproduce the biological character of the lesion.

With aid from CECR funding, Bernasconi and his team now are working to commercialize the process and make it available to others. This requires large-scale validation of the algorithms which is currently underway. “Surgery when the MRI fails to reveal obvious cortical dysplasia is one of the greatest challenges around the world,” says Bernasconi. “To identify a surgical target, these patients often undergo long and costly hospitalization with EEG probes inserted – a complication risk in itself.

“Our technology is a bit like satellite imagery. Once the computer zooms you in, you see all the detail.”

The MNI is regularly asked to supply a collaborative study has been initiated with the cognitive neuroscience and brain imaging laboratory (CNRS) in Paris, France.

SUMMARY

Dr. Bernasconi is giving new hope for untreated epilepsy patients with computer modeling to reveal previously unseen targets for surgery. Opportunities for commercialization are considerable.

PROGRESS

The first year of CECR funding has seen implementation of a software code management system. A website has been set up to receive MRI data from other epilepsy centres around the world which will add to the validation.

A collaborative study has been initiated with the Cognitive Neuroscience and Brain Imaging Laboratory (CNRS) in Paris, France.

OUTLOOK

The web-based platform is expected to gather 10 new cases per centre per year for a multi-centric validation study. Participants will include the CNRS in Paris and centres in London, New York University, Yale, and University of Melbourne. Each will also establish contacts with tertiary epilepsy centres.

Besides clinical use, opportunities for commercialization include integrating the software directly into MRI hardware systems, of interest to the three major manufacturers (Siemens, GE and Philips). Another goal is to include the technology in clinical research to provide detection and 3D visualization not currently available during surgery.
Am I going to get Alzheimer’s?

By the time you know you have Alzheimer’s, the disease is well advanced. That’s because identification is dependent upon behavior as revealed by cognitive testing such as memory tests. These symptoms become more visible as the disease progresses.

There is a huge social cost associated with Alzheimer’s. In Canada, one in 20 persons over the age of 65 – and one in four over 85 – suffers from the disease, at a cost of $5.5 billion each year in medical treatment. The numbers are lower for Parkinson’s, a similarly neurological disease, but about to rise. 85% of patients are over 65, an age group that will double in size to 23.6% of the population in 30 years.

Although no treatments exist to stop the progression of these diseases, a world-wide effort has already led to the development of drugs that promise to slow the progression. But these efforts are mitigated by the inability to detect the disease early. Some MRI and PET measurements have shown differentiation in patients but these are inaccurate in the disease early. Some MRI and PET measurements have shown differentiation in patients but these are inaccurate in the disease early. That’s because the brain’s state at those coordinates, an investigator is using assumptions modeled on a single brain 100 years ago. This effort is using assumptions modeled on a single brain 100 years ago.

The ability to predict these diseases before they show up in symptoms has two significant benefits. Early identification could be critical when therapies are finally developed, resulting in slowing the progression of the disease and reducing the cost of care. The same technology would also be instrumental in measuring the effectiveness of clinical trials of new drugs.

Dagher and his colleague Dr. Amir Shmuel propose to combine structural MRI, fMRI and EEG information in a suite of five measurements instead of only a single type of measurement. This combination of multi-modal tests is expected to be a highly accurate predictor of these diseases.

The end product will be a push-button sequence that will run on clinical MR scanners which are widely available in hospitals and private clinics. The analysis software will automatically read the files from the scanner, analyze them and report results promptly. The two investigators anticipate that modifications to the analysis software will make it applicable for a wide range of additional pathological states such as MS, schizophrenia, epilepsy and spatial neglect following stroke.

The initiative is separated into three connected projects:

**Mechanism and diagnosis of Alzheimer’s**: neuronal correlates of spontaneous fluctuations in fMRI signals and of functional connectivity at rest. Almost all first year goals have been achieved in all three projects.

**Application to health care**: Earlier start to treatment and measurement of effectiveness.

**Outlook**: Work in the second year will focus on continuing to acquire data, refining computer algorithms to determine optimum procedures and developing data on structural connections through Diffusion Tensor Imaging.

**Project**: Early diagnosis of Alzheimer’s and Parkinson’s Diseases

**Application to health care**: Earlier start to treatment and measurement of effectiveness

**Investigators**: Alain Dagher, Amir Shmuel

**Funding**: $100,000

**Commercialization potential**: High
Getting Back Your Nerves

The Central Nervous System (CNS) consists of the brain and spinal cord. It controls our thoughts, senses and movement through an incredibly complex system in which special cells, neurons, connect to each other to transmit and receive information.

Severe injuries to the CNS tend to have devastating consequences because, once ruptured, the neurons and supporting cells are unable to spontaneously regenerate and restore functional communication. The CNS environment makes things worse by sending inhibitory signals to injured CNS neurons blocking the regeneration process.

A primary candidate for blame has been RhoA, a neuronal protein that responds to inhibitory signals and is known as a “molecular switch.” But RhoA influences a wide range of cells, meaning there is likely going to be unwanted side effects of any direct manipulation of its function.

At the MNI, a team of researchers led by Dr. Alyson Fournier went back to the beginning to see just how the injured neurons were being inhibited by the CNS environment following trauma. It has identified a key protein – CRMP4 – that interacts with RhoA and successfully designed a derivative – CARIP – which promotes regeneration in cultured cells.

“This is quite unique in terms of how it acts,” says Fournier. "CRMP4 and its derivatives target a protein primarily expressed in neurons, which means it is less likely to disturb other Rho-dependent processes. We see it as a strong candidate for development." A treatment for spinal cord injury would have a huge impact. Although the numbers are small compared to other major diseases - some 40,000 cases of SCI in Canada, with 1,000 new cases each year – care is costly.

With 80% of all spinal cord injury happening to people under 30, lifetime support costs can range from $1.25 million to $5 million. A treatment for spinal cord injury would be a strong candidate for development.”

Dr. Fournier is edging closer to the holy grail of spinal cord injury treatment – getting the severed nerves to re-establish functional connections. The road ahead is long, but the rewards considerable.

SUMMARY

Dr. Fournier is edging closer to the holy grail of spinal cord injury treatment – getting the severed nerves to re-establish functional connections. The road ahead is long, but the rewards considerable.

Project: Regeneration of neurons in spinal cord injury
Application to health care: Building blocks for a therapeutic treatment of SCI
Investigator: Alyson Fournier
Funding: $100,000
Commercialization potential: High

PROGRESS

Structure function analysis of CARIP has been completed. High quality CARIP has been produced in sufficient quantity to initiate spinal cord injury study to be undertaken at the University of British Columbia (UBC).

A pilot set of experiments has been completed assessing the effects of CARIP on regeneration in an optic nerve model, in collaboration with the University of Montreal (U of M). High quality CARIP has been produced in sufficient quantity to initiate spinal cord injury study to be undertaken at the University of British Columbia (UBC). The project’s first year has been encouraging, but the volume of research ahead is considerable.

“There are good indications but it’s early days and we have a long way to go,” says Fournier. “I think we have the solution for delivery of the protein and there is definitely potential for it to serve in a combined therapy.”

“Combined therapy will almost certainly be required, because there are many inhibitors. Just working on one protein isn’t going to produce a single drug that enables complete recovery from spinal cord injury.”

Collaborative research scheduled consists of regeneration studies of retinal ganglion cells (RGCs) with U of M; spinal contusion injuries with McGill University; and the UBC studies which will focus on spinal cord transection injuries.

OUTLOOK

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The MNI’s achievements in researching the cell biology of neurons are widely recognized and it is felt today that many outstanding questions require accessing expertise in computer modeling. OER funding is being applied to a collaborative effort with the McGill community to model cell biological processes, based on several recent and successful collaborations. The project will foster interaction and establish four Fellowships to train neuroscientists and computer scientists in approaching neuronal cell biological problems.

Alain Dagher
Computational Modelling of Cell Biological Processes ($40,000)

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Edward Ruthazer
Structural Stress on Eating Behaviour ($65,000)

Obesity is a major health concern that has reached epidemic proportions in Canada and in other countries. The effect of medication is uncertain because obesity is not simply a disease of chemistry. This study focuses on how the perception and experience of food and eating may impact brain chemistry and promote overeating. In particular, it seeks to decipher if and how stress plays a part. A better understanding may lead to preventive strategies, both pharmacological and behavioural, to curb this epidemic.
Every day in Canada, another 40 people join the 430,000 diagnosed with epilepsy. In one-third, seizures cannot be controlled by medication or the side-effects are debilitating. However, in all but the most severe cases, the seizure itself is not the key issue.

"Epileptic seizures are rarely the big event many people imagine," says Dr. Jean Gotman. "It’s more likely a disassociation with your surroundings, maybe a blackout. The real problem lies in not knowing when it will happen."

Gotman has spent the past 37 years – since his arrival at the MNI – investigating epilepsy. The ultimate goal, he says, would be a device similar to a cardiac pacemaker that monitors the nervous system, identifies an oncoming seizure and modifies the condition to prevent or arrest it.

"Right now, the sensors work in saline water but not in living tissue," says Gotman. "However, they seem to be solving the key issue.

"Our focus now is on determining the optimum size of the electrode to use, because this decides what information you receive, or whether you even hit the target," says Gotman. "It’s a trial and error procedure so it takes a lot of time."

The second research program uses new sensors to measure local concentrations of oxygen and pH – a new set of variables under study in patients with epilepsy. Experimental evidence and clinical observations have pointed to an increase in oxygen consumption in the seconds or minutes leading to a seizure.

A portion of the funding is directed to Professor Vamsy Chodavarapu of the McGill University Electrical and Computer Engineering Department who is leading the development of the prototype sensors.

"Right now, the sensors work in saline water but not in tissue," says Gotman. "However, they seem to be solving the problem and we’ll go back to that research when they do."

**SUMMARY**

A big problem facing patients with epilepsy lies in not knowing when a seizure will occur. Dr. Gotman is working on finding elusive biomarkers that would indicate an imminent attack and a French firm has already expressed commercial interest.

**PROGRESS**

Evaluation of a range of electrode sizes was completed, demonstrating surprisingly that HFOs were not recorded better with smaller rather than larger electrodes, given their original observation at the single cell level. The study shows standard electrodes may be adequate.

Experimentation with oxygen and pH sensors has led to a redesign of the probes. An international company, Dixi Microtechnique of France, has expressed interest in the commercialization potential.

An initial program to research seizure arrest has been set aside pending additional funding.

**OUTLOOK**

The evaluation of the optimal size of electrode will continue in humans and in a chronic rat model of epilepsy. Once a method of automatic detection has been developed, research will be expanded in scope to determine whether seizures may result from synchronization of a network of HFO generators.

A technique for monitoring oxygen concentration over longer periods of time will be researched in animals. If this provides evidence of approaching seizures, the technology will be developed for human recording.
Building a Better Roadmap

Each year, some 200 of the thousands of Canadians requiring neurosurgery end up at the Montreal Neurological Hospital. These patients require resection of lesions that are extremely close to functional areas of the brain, critical to movement, vision, sensation or language. Their condition often will have been deemed inoperable due to the location of the lesion.

To remove the most diseased tissue without intruding upon critical brain areas, the surgeon must fully understand complex relationships between anatomy, blood vessels, functional regions and pathological features. It would be a huge advantage if functional neuroimaging technology from the lab could be made available right in the operating room, integral to neuro-navigation technology.

But this would mean somehow bringing together expertise from imaging technology, computer engineering, statistics, cognitive neuroscience, neuro-radiology and neurosurgery — all taking place on different platforms in various labs around the complex.

“We have all these state-of-the-art procedures, but everyone works on their own. Once we bring them all together, we will be able to offer the technique to other hospitals and institutes across Canada.”

Integrating the various technology outputs is an ambitious undertaking. For example: magnetic resonance images (MRI) supply intricate detail of a tumour and surrounding anatomy, blood flow adjacent to the tumour is recorded by positron emission tomography (PET), regions of functional importance are identified by functional magnetic resonance imaging (fMRI), blood vessels are mapped in detail by an angiogram.

Integrating all this data in a form of value in neuro-navigation requires a software package that is easy to use and operates on a system-independent platform.

The rewards of success would be significant. With this knowledge, the surgeon can not only plan the surgery more precisely and confidently but even discuss options with the patient.

“We see this as an important development in advancing neurosurgery, but it is the kind of project which was not eligible for any of the CECR grants,” says Denise Klein, who is leading the project.

We are currently the only centre in Quebec that has the potential to offer an integrated pre-surgical mapping service under one roof,” says Denise Klein, who is leading the project.

Summary

Dr. Klein is aggregating the powerful laboratory imaging techniques available throughout the MNI and planning to deliver a real-time, integrated output in the operating room. Commercial demand for the integrated solution and software would be considerable.

Progress

All first year goals have been met. The project has strengthened existing collaborations and initiated new ones, bringing together individuals with expertise from brain imaging, neuro-radiology, neuropsychology, neurology, and neurosurgery. Some 42 patients have gone to surgery with the aid of these newly integrated, pre-mapping tools.

In the year before the project began, the MNI could only afford to test and document seven patients. It is now processing two a week.

Outlook

The emphasis in the second year is on data reporting and management and integrating the information into a single software platform that will permit use in the clinical domain. A universal database with common visualization tools will enable all units within The Neuro to work with patient data. This will provide the transition from pre-operative planning to real-time neurosurgical intervention.

Development of the software will be of high commercial significance and development of the unit itself at the MNI may attract financial endowments from donors.
Tapping, 1, 2, 3, 4.

Rapid tapping with a stylus on a metal plate is a test often used to evaluate motor speed and coordination in patients with a neurological disease such as Multiple Sclerosis. Many years ago, a research team at the MNI led by Dr. Gabriel Leonard demonstrated that rapid repetitive tapping with one hand is mainly sensitive to primary motor brain areas and the corresponding motor pathways.

The team applied more intricate tapping tasks for one and two hands that contributed much more sensitive measures of disability. This test has become widely used at the MNI and also in several large-scale studies. “The trouble is these are still mechanical tests, and accurate reporting is difficult,” says Leonard. “The only record of performance is by the person giving the test, who has to remember and note all the incorrect sequences.”

Leonard now has addressed the need for a reliable and accurate tapping apparatus capable of creating an objective record. Working with a programmer and hardware designer, his team has built a prototype computer interface, together with software, that is less cumbersome and that accurately reports all scores.

Significant advances include:
- It documents all errors made, including misses, perseverances, and sequential errors.
- It delivers objective scores for four subsets of test pattern using each hand and both hands, permitting wider ranging analysis.
- It will compare test scores to a representative (normal) control group.
- It will also provide mean scores for subjects with neurological illnesses, e.g., MS, epilepsy, post concussion syndrome, etc.

“It’s basically the same process that Gabriel originally used in 1988,” says research associate Dr. Joelle Crane. “But putting it on a computer creates a vastly superior tool. It’s a big advance.”

The test has many applications. Together with imaging it could provide insight to the surgeon as to the location of brain damage, or the extent of injury in an accident. It is a means of accurately measuring progress in rehabilitation or of objectively assessing effects of a specific drug or treatment. The test can be administered by clinical assistants or a General Practitioner. It can be employed for diverse measurements such as assessing dexterity following carpal tunnel damage or determining whether the effects of aging are augmented by a brain deficiency.

Leonard believes the potential for commercialization is high and has already received interest from colleagues locally and abroad. There are no commercially available tests to measure sequencing of arm and hand movements, including out-of-phase coordinated bi-manual movements.

SUMMARY

Dr. Leonard is putting a new twist on established technology to produce a superior device for testing motor skills in patients with neuromuscular or neurological disease. The prototype is testing well and commercial development is anticipated in 2010-2011.

PROGRESS

The first year of the project has seen completion and validation of the prototype. Some 50 pilot subjects have been tested to confirm the correct operation of the tapping machine and several user-friendly internet forms have been designed (e.g., medical and handedness questionnaire).

OUTLOOK

The major task ahead is the data collection and recording the performance of healthy people. The normative study will require data from approximately 2,000 subjects ranging in age from 6 to 90; the usual number used in commercially available neuropsychology tests.

The data gathering, followed by statistical analyses, software adjustments and a published paper, will take two years to complete. Leonard hopes to announce the new tapping test in mid-year 2010 at selected international neuroscience gatherings to communicate the potential to other neuroscientists, clinicians and representatives of pharmaceutical companies.
Understanding the cellular basis of disease is one of the revolutionary developments in neurological research. Today it is understood that schizophrenia, Parkinson’s, MS, ALS and many others are not diseases of the mind or brain, but of the cells that underlie all brain functions.

Many MNI investigators are focused on researching disease processes at the level of cells and disease-causing proteins. A fundamental challenge they face is identifying specific proteins present in the various cells of the human body.

The most efficient way to detect specific proteins is through the use of antibodies, a primary tool of the body’s immune system. Antibodies are incredibly specific in identifying and attracting any foreign or unwelcome protein.

Antibodies can be designed to target a specific protein. However, they are difficult and costly to produce and have a high failure rate, all of which has led to development of a large retail trade. At the MNI, Dr. Peter McPherson’s lab has been creating custom antibodies for some time. Frustrated by the difficulties and inherent in standard approaches, McPherson and a colleague brainstormed a novel process by combining elements of proven procedures, creating a hybrid, which showed itself to be significantly faster, simpler and cheaper. With built-in validation from the experience of MNI “customers”, a highly profitable catalogue of products is being assembled for commercial utilization.

“We were spending over $20,000 a year on commercial antibodies for our own research,” says McPherson. “Our hybrid discovery makes it viable and much, much cheaper to do it in-house.”

With CECR funding, McPherson set up a separately staffed “Antibody Core” within his own lab. The facility produces custom antibodies for investigators at the MNI and, recently, for others in the McGill health community.

“If we just stopped here, the CECR funding would have created a profitable enterprise that will be self-sustaining for the foreseeable future,” says McPherson. “But, in fact, antibody production and commercialization model has very high potential.”

That’s because whereas McPherson’s procedure greatly simplifies antibody production, the validation of the antibodies remains difficult because of the need for the right biological testing environment. Since the McPherson lab is producing custom antibodies for colleagues, the work of these investigators becomes the validation of the product. The solution was to make the commercialization process a shared one.

“For each antibody, we sign a Report of Invention which shares inventorship between the centre and the investigator,” says McPherson. “We can build up a big catalog this way.”

The activities of the Antibody Core are being expanded. A website is being established for promotion and a second technician is being hired.

OUTLOOK

The Antibody Core has undertaken projects for 12 investigators. Eight antibodies undertaken prior to CECR funding have been commercialized. Several of the antibodies generated since the initiation of the core are now in the process of being commercialized.

Chronic pain affects the quality of life and productivity of millions of Canadians. Effective treatment is seldom available and the solution lies in better translation of basic research findings on pain mechanisms into innovative drug development. This CECR project is focused on the role of TRPC ion channels in the cellular mechanisms of chronic pain. The goal is to validate TRPC3 channels as pharmacological targets that modulate the sensitization of DRG neurons known to participate in inflammatory and neuropathic pain and, secondly, to target TRPC3 activity in vitro and in vivo.
When the MNI first opened its doors 75 years ago, much of the discovery in medical science was accomplished through post-mortem examination. Today, the most sophisticated pathologies are identified and studied in vivo through the extraordinary power of medical imaging and measuring equipment. This is excellent news for the patient, who today can reasonably expect to have his or her condition treated and life prolonged, rather than dissecting a dead one. “Our imaging equipment represents an investment of over $35 million,” says Bruce Pike, Director of the McConnell Brain Imaging Centre. “The service contracts alone cost close to $2.5 million a year.”

The BIC, which is marking its 25th year, is considered one of the top three brain imaging establishments in the world. The MNI’s Brain Imaging Centre has a long history of developing novel methods and commercializing them or translating them into routine research clinical use. These include innovative PET scanners, neurosurgery planning software and computerized imaging analysis tools.

PROGRESS

Service contracts have been finalized for our three Positron Emission Tomography scanners, one of which is a state-of-the-art High Resolution Research Tomography (HRRT) scanner. A service contract renewal for the IBA cyclotron was successfully negotiated. A Master Research Agreement for the MRI research program will allow us full access to Siemens scanner code for our own R&D.

Core computing and data storage (500TB) facilities have been restructured, including transition to Linux OS, and a new fee-for-service model implemented.

OUTLOOK

We are building on a reputation for reliability in providing radionuclides (18F-FDG) to the PET program in the McGill University Health Centre. This commercial output of our cyclotron brings in important revenues. We have been approached by a large radionuclide distribution company and will explore opportunities for partnership. This will likely require further investment in our production capability.

RESEARCH REPORTS

APPLIED NEUROSCIENCE AND COMMERCIALIZATION

Phil Barker

Targeting Neurito Growth Inhibitor Receptors to Promote Regeneration after Injury

($75,000)

The development of drugs that will enhance neuron repair after spinal cord injury is one of the most sought-after research goals. This project brings together an impressive representation of the expertise available at the MNI with investigators experienced in biochemistry, signalling, cell-based models of neurite inhibition and pre-clinical models of spinal cord regeneration. First-year work is promising and the project is seen as an example of the high-impact, high-payoff project for which the CECR funding is suited.

Tim Kennedy

Identification and Characterization of Novel Compounds to Inhibit Cell Migration

($75,000)

Dr. Kennedy and his team previously identified a fragment of Netrin 1 that inhibits cell movement, without the attractive function of the full-length protein. The goal of the current project is to synthesize peptides with this minimal sequence in order to develop compounds with favourable drug-like properties that could inhibit cell movement. Diseases in which abnormal cell migration is an important factor include the metastasis of tumour cells in various cancers, and the abnormal growth of blood vessels in diseases which are a leading cause of blindness. Importantly, the lab has evidence that tumour cells and vascular cells have the receptors required to respond to the proposed compounds, indicating that they should have clinical utility.

Amit Bar-Or, David Colman

Initiating Targets and Prognostic Markers of MS in Pediatric-Onset

($180,000)

Canadian children suffer one of the highest rates of Multiple Sclerosis in the world. MS is the leading cause of neurological disability in young adults in the Western hemisphere and is caused by repeated attacks on the central nervous system by the body’s immune system. Although treatments are able to partially reduce attacks, doctors are unable to tell at the time of the first attack whether this is isolated or whether it will progress into MS. This project seeks to define early molecular targets of the disease and identify biomarkers that can be used to predict the onset of MS.

SUMMARY

The MNI’s Brain Imaging Centre has a long history of developing novel methods and commercializing them or translating them into routine research clinical use. These include innovative PET scanners, neurosurgery planning software and computerized imaging analysis tools.

Project: Imaging innovation and leadership

Application to health care: Making available world-class medical imaging and analysis

Investigator: Bruce Pike

Funding: $500,000

Commercialization potential: Medium

Making the Best Impression

Research Imaging Here.

Members, mostly from the McGill community, do their share of the top three brain imaging establishments in the world. When the MNI first opened its doors 75 years ago, much of the discovery in medical science was accomplished through post-mortem examination.
Transcranial Magnetic Stimulation (TMS) is a recent and exciting development in neurology; the only technique to allow direct manipulation of neurons non-invasively. Much has been learned about what the technology can do, but a lot less about how it happens. It seems the science got left behind.

The application of TMS to the human brain for therapy and for understanding cognition got ahead of the experimentation needed to understand how TMS works. “The potential is being applied before the base of knowledge has been established,” says Dr. Amir Shmuel. Shmuel was recruited from Germany and heads up a multidisciplinary team on TMS. He is focused on supplying the missing scientific analysis on which four colleagues will build specific clinical applications.

The TMS procedure involves placing a wire coil close to the head and inducing a pulsed magnetic field which passes through the skull and excites neurons in the brain, producing a measurable result.

To discover what happens inside the brain, Shmuel will use TMS to “knock-out” activity in the region is “knocked-out” by TMS and perforation in both diagnosis and therapy.

Because TMS is capable of increasing, decreasing or actually de-activating the functional activity, it delivers a new dimension in both diagnosis and therapy. Diagnosis: while functional MRI indicates which area of the brain is active during a particular task, it does not indicate whether that activity is actually involved in the task. But if the activity in the region is “knocked-out” by TMS and performance of the task suffers, it indicates the region is in fact being used and to what extent.

Therapy: repetitive application of TMS, or rTMS, has been shown to decrease neuroinflammation after the stimulation has been stopped. This suggests that specific behaviour of the brain could be modified and remain modified until another treatment is needed, promising important breakthroughs in many neurologically related diseases such as recovery from stroke, depression, chronic pain, and others.

Shmuel’s colleagues are pursuing four of these possibilities:

- **Amblyopia** - (Chris Pack), Amblyopia is an untreatable disorder affecting 1%-5% of the population and a leading cause of vision loss in young children. It is now known to be caused by abnormalities in the visual cortex which could be modified by TMS.

- **Auditory cortex and tinnitus** – (Robert Zatorre). Tinnitus is a chronic auditory hallucination such as a loud ringing in the ear and has surfaced as a frequent complaint of Iraq war veterans. TMS is seen as a promising treatment by reducing the hyperexcitability in the auditory parts of the brain.

- **Cognitive recovery post-stroke** - (Lesley Fellows). Hemi-Spatial Neglect is induced by stroke and leaves the patient with no awareness of anything on one side of his field of vision. There is no established treatment. It is hoped that TMS can address the under-activity of the damaged right hemisphere of the brain’s attention system or reduce a counter-productive over-activity in the intact left hemisphere.

- **Surgical planning for tumour removal** – (Michael Petrides and Rolando Del Maestro). Increasing or decreasing activity in areas of the brain next to the tumour will greatly reduce uncertainty in planning the surgery and lessen the likelihood of damage to other cognitive functions.

**Summary**

Transcranial Magnetic Stimulation is an exciting advance, but more is known about what it does than how it does it. Dr. Shmuel is addressing the lack of experimentation to reveal the mechanisms of TMS, while colleagues develop clinical applications with both translational and commercial significance.
Targeting Medicine with Molecular Diagnosis

With molecular diagnostics, a key technology in “targeted medicine”, populations can be identified that are predisposed to certain diseases, leading to earlier intervention and better therapies.

“There is a particular need for molecular diagnosis in neurology, because a large number of diseases are hereditary, caused by genetic mutations”, says Michael Sinnreich. “Not only does it help define a precise treatment – or prevent the wrong treatment – but the knowledge is critical in family planning and counseling for an inheritable disorder.”

Sinnreich and Dr. Eric Shoubridge co-direct the new Molecular Diagnostic Laboratory for Neuromuscular Diseases. Shoubridge is an internationally renowned specialist in molecular genetics of mitochondrial diseases. Sinnreich and Shoubridge were each pursuing their own specialty when Sinnreich began to consider the need for a more comprehensive capability within the MNI.

The MNI is the reference centre for neurological diseases in Canada. Patients are referred from across Quebec, Canada and North America for investigation. “Genetic diagnosis is not easy to obtain in Quebec”, he says. “It’s cumbersome and costly. Either you send a test to very expensive commercial labs out of province, or you send it to specialized research labs that only do one type of test and takes six months. Since we do a lot of genetic testing here at the MNI, it seemed to me a clear case for a well structured facility of our own.”

With a start-up budget from CECR funding, the Laboratory has been sufficiently successful to warrant increased funding in Year 2. The lab has generated sufficient revenue on a cost-recovery billing basis to enable the hiring of a second technician. Most initial tests were done for clinicians at MNI or within the MUHC, but the service is starting to attract business from a wider circle.

The MNI is now looking at a more expanded capability for the Laboratory: a new study of the diagnostic market anticipates compound annual growth of 13% for molecular diagnostics over the next three years.

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Neuropolis has an estimated budget of $7 million and a target for completion in 2 years. In September 2009, the MNI and the NFB will be seeking partners to participate in the production and distribution of the film. This partnership initiative will include discussions with the National Science Foundation in the United States, the IMAX Corporation and other corporations, as well as foundations and government agencies.

McGill Integrated Neuroscience Program and Student Rotation Program
The McGill Integrated Program in Neuroscience (IPN) is a new initiative, in line with McGill University’s Strategic Plan to attract top graduate students. Montreal has a very high concentration of neuroscientists, but they are spread out through different departments, hospitals and research institutes. The IPN is a multi-disciplinary, inter-departmental program that will bring together all graduate training in neuroscience currently under the McGill umbrella, and will offer prospective students a single, consolidated program through which to apply for and attain their MSC or PhD in neuroscience. The IPN has evolved from the Graduate Program in Neuroscience, which was already offering graduate degrees in neuroscience. All aspects of the student experience, including the program’s website, application and supervisor selection procedures, tracking the attainment of milestones, perception of belonging to a McGill program, and student awards, are being improved over previous systems. The IPN will also offer a Rotation Program for outstanding students who wish to try their skills in several different laboratories for their first year, before committing to a supervisor for the rest of their graduate work.

Integrated Program in Neuroscience Retreat (September 17-19, 2009)
The inaugural Integrated Program in Neuroscience (IPN) Retreat will be an unprecedented opportunity for McGill researchers, from all disciplines of neuroscience, to come together and share their work with one another. Attendance at the two day event is mandatory for all new students admitted to the IPN, and all labs of IPN supervisors are also invited. With poster sessions (with up to 200 posters), overview talks and themed sessions, McGill’s contribution to the world of neuroscience research will be showcased at the Retreat. Additionally, other scheduled activities will encourage interaction among students, postdoctoral Fellows and principal investigators representing the full depth and breadth of McGill neuroscience. Overall, we expect the Retreat to be the ideal launch for the IPN, bringing all members together, and cementing their perception of belonging to a cohesive neuroscience program. In future years, the Retreat will become an annual event and serve as a highlight of the IPN.

Media Relations and Public Outreach and Education
An amount of $355,000 of the CECR Award was set aside in 2008-2009 to fund a number of endeavours that aim to increase public awareness of The Neuro, its scientific and clinical activities and contribution to health care. Branding and outreach activities include print ads for magazines and public locations, and aim to ensure a written and visual presence in the lay public’s mind. The ads have been used to leverage donations of ad space worth approximately $150,000 in 2008-2009.

The Neuro celebrates its 75th anniversary in 2009. A Coordinator has been hired to develop material and to plan 75th anniversary events, thereby ensuring that The Neuro enjoys continued and appropriate visibility.

PUBLIC OUTREACH AND ENGAGEMENT ACTIVITIES
Funds from the CECR Award to the MNI have been allocated for educational and outreach activities. The initial investment of CECR funds is expected to leverage additional funds from the private sector and to lead to long term educational benefits, including transferring knowledge and inspiring the next generation of scientists.

Neuropolis
In collaboration with the National Film Board of Canada (NFB), the MNI is developing an immersive, 3D IMAX-type motion picture on neuroscience that features the work of scientists at the MNI and at other universities and centers around the world. The main purpose of the film is to spark curiosity and to inspire a new generation of young people to be excited about science, and particularly neuroscience. Given the inherently interesting discoveries about how the brain and nervous system work, viewers will be drawn into a story of who scientists are and how they think about scientific questions, and see young people from diverse backgrounds who are making a career in the field of science.

Using a very accessible metaphor of the nervous system as a city, the film entitled Neuropolis will help viewers to understand and to appreciate the complexity of the nervous system, the nature of communication among its components and the degree of specialization in different regions of the brain. In addition, some of the most striking discoveries in neuroscience will be woven into the film, such as new findings about the plasticity of the adult brain that have changed the way we think about learning and recovery from injury. More than one hundred hours of interviews with scientists have been conducted and edited, and the film conference has been developed into a fully realized video story board. For the three dimensional effects, the NFB is using the SANDIE (Stereo Animation Drawing Device) system developed by the entertainment technology company IMAX Corporation, and installed at NFB on a pilot basis. The value of this real time 3D drawing technology and other technologies, such as computational photography, will be demonstrated and disseminated through the execution of this film, which will add an additional dimension to the knowledge translation aspect of this project.

McGill, a world leader in neuroscience, has already attracted a steady stream of international visitors, students and post-doctoral fellows. One of the most popular events is the annual panel discussion ‘Pathways to Neuroscience’, which is now developing the Neuropolis film. The film will bring together all graduate training in neuroscience currently under the McGill umbrella, and will offer prospective students a single, consolidated program through which to apply for and attain their MSC or PhD in neuroscience. The IPN has evolved from the Graduate Program in Neuroscience, which was already offering graduate degrees in neuroscience. All aspects of the student experience, including the program’s website, application and supervisor selection procedures, tracking the attainment of milestones, perception of belonging to a McGill program, and student awards, are being improved over previous systems. The IPN will also offer a Rotation Program for outstanding students who wish to try their skills in several different laboratories for their first year, before committing to a supervisor for the rest of their graduate work.

Institution and International Fellows Program
The CECR Fellowship supports research and study in clinical and basic neuroscience. The MNI has awarded a total of 10 Fellowships in 2008-2009:

- 9 Fellowships are funded at $40,000 each for two years;
- 1 Fellowship is funded at $15,000 for the first year and at $10,000 for the second year.

Branding and outreach activities include print ads for magazines and public locations, and aim to ensure a written and visual presence in the lay public’s mind. The ads have been used to leverage donations of ad space worth approximately $150,000 in 2008-2009.

The Neuro celebrates its 75th anniversary in 2009. A Coordinator has been hired to develop material and to plan 75th anniversary events, thereby ensuring that The Neuro enjoys continued and appropriate visibility.

Development and maintenance of web-based performance monitoring resources
The MNI has established an on-line system that can be securely accessed via the web and that allows MNI faculty to apply for funding. This web-based application also allows successful applicants to provide quarterly updates that show progress toward milestones, and to provide information on commercial developments as well as on trainees and staff who have been hired.
Our overall objectives defined in 2008-2009 form part of a long-term strategy for effective use of the CECR Award over a three-year period and have been maintained for 2009-2010. Our plan for the second year of the CECR will help us pursue activities that were initiated in 2008-2009 and to identify new projects for funding.

The application and review process that was established in 2008-2009 has been maintained, and progress against initial goals and milestones is a key requirement for continued funding. Clinicians and researchers have been invited to apply for funding through the MNI CECR: some of these applications represent renewals of projects funded in the first year, but we also considered new applications that target areas for commercial or translational innovations. Portions of the Award have also been set aside for development of highly-qualified personnel and for expansion of our public outreach and engagement activities.

**Planned expenditures for 2009-2010 are defined as follows:**

<table>
<thead>
<tr>
<th>Investigator Initiated Programs</th>
<th>$995,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuroengineering</td>
<td>$545,000</td>
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<tr>
<td>Translational neuroscience</td>
<td>$1,315,000</td>
</tr>
<tr>
<td>Applied neuroscience and rapid commercialization</td>
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<tr>
<td>Clinical trials support</td>
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<tr>
<td>Public Outreach and Engagement</td>
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<td>Fellowship Program</td>
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<tr>
<td>McGill Integrated Neuroscience Program</td>
<td>$150,000</td>
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<tr>
<td>Media relations and outreach</td>
<td>$150,000</td>
</tr>
<tr>
<td>Intellectual property protection and business development</td>
<td>$150,000</td>
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<tr>
<td>Administration</td>
<td>$50,000</td>
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<tr>
<td><strong>TOTAL</strong></td>
<td>$5,160,000</td>
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</tbody>
</table>

Our short term goals for 2009-2010 focus on reviewing Year 2 applications and initiating funding. Our medium term goals are to facilitate the growth of commercial ventures that were initiated in Year 1, and to ensure appropriate management and governance structures for these entities. The Internal Review Committee, the Commercialization Committee and the Centre of Excellence Advisory Board will ensure, through their respective mandates, that management of the MNI CECR Award is efficient, fair and transparent, and that funding is used towards stated objectives.
Auditors’ report

To the management of the Royal Institution for the Advancement of Learning

At the request of the Royal Institution for the Advancement of Learning (McGill University) (the “University”), of which the Montreal Neurological Institute of McGill University (the “Institute”) is a department, we have audited the statement of revenue and expenses for the period from June 1, 2008 to May 31, 2009 (the “Schedule”) of the Institute in connection with the Funding Agreement signed with the Minister of Industry. This financial information is the responsibility of the management of the Institute and of the University. Our responsibility is to express an opinion on this financial information based on our audit.

We conducted our audit in accordance with Canadian generally accepted auditing standards. Those standards require that we plan and perform an audit to obtain reasonable assurance whether the financial information is free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial information. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial information.

In our opinion, the Schedule presents fairly, in all material respects, the revenue and expenses of the University for the year ended May 31, 2009 in accordance with the University’s reporting requirements under the Funding Agreement with the Minister of Industry.

November 25, 2009

Samson Belair/ Deloitte & Touche s.e.n.c.r.l.

1 Chartered accountant auditor permit no 22220

McGill UNIVERSITY
FUNDING AGREEMENT WITH
THE MINISTER OF INDUSTRY

Statement of revenue and expenses
for the period from June 1, 2008 to May 31, 2009

<table>
<thead>
<tr>
<th>Revenue</th>
<th>$15,000,000</th>
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<tbody>
<tr>
<td>Minister of Industry</td>
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<tr>
<td>Interest earned on revenue</td>
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<table>
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<th>Expenses</th>
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<td>Salaries</td>
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<td>Fringe benefits</td>
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<td>Material and supplies</td>
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<td>Contract and consultant services</td>
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<td>Travel</td>
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<td>Equipment</td>
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<td>Miscellaneous</td>
<td>97,360</td>
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<td></td>
<td>2,906,485</td>
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</table>

| Excess of revenue over expenses  | $12,412,534 |

The following information is presented in accordance with our Funding Agreement:

Article 8.2.a.i – The median value for the salary range of executive and senior staff members is $130,427
Article 8.2.a.ii – The median value for the salary range for employees earning more than $100,000 is $134,272

The CECR Award was not used to fund these salaries.
The following projects and initiatives were accepted by the Internal Review Committee for funding in 2008-2009. The Internal Review Committee complied with McGill University's Policy on Conflict of Interest and Duty of Loyalty in the evaluation of proposals submitted for CECR funding and in decisions with respect to funding of projects.

<table>
<thead>
<tr>
<th>INVESTIGATOR</th>
<th>BIOLOGICAL BASIS OF NEUROLOGICAL DISEASE</th>
<th>FUNDING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edward Ruthazer</td>
<td>Computational modeling of cell biological processes</td>
<td>$ 40,000</td>
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<tr>
<td>Michael Petradas</td>
<td>Creation of the MINI probabilistic architectonic atlas of the human cerebral cortex</td>
<td>$150,000</td>
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<tr>
<td>Viviana Sziklas</td>
<td>fMRI study of acquisition and retrieval of pseudowords and designs in temporal lobe epilepsy</td>
<td>$ 60,000</td>
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<tr>
<td>Jean-François Clouier, Stefano Stitiflou</td>
<td>MINI Resource Centre for Mouse Models (MRCMM)</td>
<td>$125,000</td>
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<tr>
<td>Thomas Stroh</td>
<td>Multi-colour super resolution imaging of fluorescently tagged proteins</td>
<td>$ 30,000</td>
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<tr>
<td>Edward Fon</td>
<td>The cell biology of Parkinson’s disease</td>
<td>$120,000</td>
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<tr>
<td>Alain Dagher</td>
<td>The effects of stress on eating behaviour and brain activity: a functional Magnetic Resonance Imaging (fMRI) study</td>
<td>$ 65,000</td>
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<tr>
<td>Phil Barker</td>
<td>The Joint MINI-BRI Protein Production Facility</td>
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<tr>
<td>Thomas Stroh</td>
<td>Microscopy Core Services</td>
<td>$115,000</td>
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<table>
<thead>
<tr>
<th>INVESTIGATOR</th>
<th>NEUROENGINEERING</th>
<th>FUNDING</th>
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<tbody>
<tr>
<td>Eliane Kobayashi</td>
<td>Application of magnetoencephalography in the assessment of the epileptic focus</td>
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<tr>
<td>Andrea Bencosme</td>
<td>Automated lesion detection in pharmacoresistant epilepsy</td>
<td>$100,000</td>
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<tr>
<td>Robert Zatorre</td>
<td>Deaf-blindness: cross-modal reorganization and cochlear implant proficiency</td>
<td>$ 20,000</td>
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<tr>
<td>Christopher Pack, Abbas Sadikot, Amir Shmuel</td>
<td>MINI Unit for investigating mechanisms of deep brain stimulation therapy in primate models</td>
<td>$150,000</td>
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<tr>
<td>Dan Gauthier</td>
<td>Multielectrode arrays in the study of perception, memory, cognition and the control of prosthetic devices</td>
<td>$100,000</td>
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<tr>
<td>Jean Gotman</td>
<td>Seizure prediction, detection and arrest</td>
<td>$100,000</td>
</tr>
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<table>
<thead>
<tr>
<th>INVESTIGATOR</th>
<th>APPLIED NEUROSCIENCE AND COMMERCIALIZATION</th>
<th>FUNDING</th>
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<tbody>
<tr>
<td>Mirko Diksic</td>
<td>A new radioguid for monitoring of patients with Alzheimer’s disease</td>
<td>$100,000</td>
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<tr>
<td>Peter McPherson, Michael Sinnett, Eric Shoubridge</td>
<td>Antibody and lentiviral resources for neuroscience research</td>
<td>$200,000</td>
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<tr>
<td>Michael Sinnett, Eric Shoubridge</td>
<td>Molecular Diagnostic Laboratory for neurological diseases</td>
<td>$ 75,000</td>
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<tr>
<td>George Karpf, Josephine Huitem-Antbuglu</td>
<td>Preparations for dystrophin gene replacement for the therapy of dystrophin deficiency</td>
<td>$ 65,000</td>
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<tr>
<td>Alix Fournier</td>
<td>Targeting CRMP4b for neuronal repair</td>
<td>$100,000</td>
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<tr>
<td>Philippe Seguela</td>
<td>TRPC channels in neuropathic pain: from cellular physiology to novel therapeutic targets</td>
<td>$ 75,000</td>
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<tr>
<td>Phil Barker</td>
<td>Targeting neuropeptide growth hormone receptors to promote regeneration after injury</td>
<td>$ 75,000</td>
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<tr>
<td>Gabriel Leonard</td>
<td>A new computerized device to measure simple and complex hand and arm movements</td>
<td>$ 60,000</td>
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<tr>
<td>Tim Kennedy</td>
<td>Generation and characterization of novel compounds to inhibit cell migration</td>
<td>$ 75,000</td>
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<tr>
<td>Amit Bar-Or, David Coiman</td>
<td>Identification of novel initiating targets and prognostic markers of MS in pediatric-onset disease</td>
<td>$180,000</td>
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<tr>
<th>INVESTIGATOR</th>
<th>TRANSLATIONAL NEUROSCIENCE</th>
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<tr>
<td>William Feindel</td>
<td>Cost-effective analysis of the Montreal Procedure for surgical cure of temporal lobe seizures</td>
<td>$ 40,000</td>
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<tr>
<td>Alain Dagher</td>
<td>Early diagnosis of Alzheimer’s and Parkinson’s Diseases using MRI measurements</td>
<td>$100,000</td>
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<tr>
<td>Bruce Pike</td>
<td>Imaging innovation and translation</td>
<td>$600,000</td>
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<tr>
<td>Amir Shmuel</td>
<td>Clinical applications of non-invasive manipulation of neuronal excitability</td>
<td>$120,000</td>
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<tr>
<td>Denise Klein</td>
<td>Presurgical functional brain-mapping Unit</td>
<td>$150,000</td>
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<tr>
<td>Rolando Del Maestro</td>
<td>The Brain Tumour Research Centre translational research initiative</td>
<td>$ 65,000</td>
</tr>
<tr>
<td>Lesley Fellows, Marilyn Jones-Gotman, Alain Pirot</td>
<td>The MINI cognitive neuroscience testing resource</td>
<td>$100,000</td>
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<tr>
<td>David Sinclair</td>
<td>Excorial Laser-Assisted, Non-occlusive Anastomosis (ELANA): an innovative revascularization technique in the treatment of occlusive cerebrovascular disease</td>
<td>$ 75,000</td>
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<th>INVESTIGATOR</th>
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<tr>
<td>Amit Bar-Or</td>
<td>Experimental Therapeutics</td>
<td>$250,000</td>
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<tr>
<td>Angela Gange</td>
<td>The MINI Epidemiology and Biostatistics Unit for Clinical Research</td>
<td>$100,000</td>
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<td>Dara Trojan</td>
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<th>MANAGER</th>
<th>OUTREACH AND ENGAGEMENT</th>
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<tr>
<td>Thomas Gevas</td>
<td>Institute and International Fellows Program</td>
<td>$400,000</td>
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<tr>
<td>Thomas Gevas</td>
<td>McGill Integrated Neuroscience Program</td>
<td>$ 60,000</td>
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<tr>
<td>Thomas Gevas</td>
<td>Symposia and Inaugural Retreat - Integrated Neuroscience Program (Conference series)</td>
<td>$ 10,000</td>
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<tr>
<td>Sandra McPherson</td>
<td>Media relations and public outreach and education</td>
<td>$325,000</td>
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<tr>
<td>Ellen Peterson</td>
<td>Expanding Neuro-Patient Resource Centre Outreach</td>
<td>$ 30,000</td>
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<tr>
<td>Carol Wiers, William Feindel</td>
<td>Neuro History Project</td>
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<tr>
<th>MANAGER</th>
<th>INTELLECTUAL PROPERTY AND BUSINESS DEVELOPMENT</th>
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<tr>
<td>Thomas Gevas</td>
<td>Intellectual property protection</td>
<td>$130,000</td>
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<tr>
<th>MANAGER</th>
<th>ADMINISTRATION</th>
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<tbody>
<tr>
<td>Thomas Gevas</td>
<td>Administration costs</td>
<td>$100,000</td>
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The following projects and initiatives were accepted by the Internal Review Committee for funding in 2008-2009. The Internal Review Committee complied with McGill University’s Policy on Conflict of Interest and Duty of Loyalty in the evaluation of proposals submitted for CECR funding and in decisions with respect to funding of projects.
**CENTRE OF EXCELLENCE ADVISORY BOARD**

**Mandate**

To provide global oversight on whether the MNI Centre of Excellence in Commercialization and Research Award is meeting the goals and terms of the agreement and whether the funding initiatives align with MNI strategic goals.

**Membership**

Jacques Bougie, O.C, holds law and business degrees from the Université de Montréal and HEC-Montréal. Mr. Bougie was made an Officer of the Order of Canada in 1994 and received an honorary doctorate from the Université de Montréal in 2001. Mr. Bougie is currently a director of Nova Chemicals Inc., AbitibiBowater Inc., CSL Group Inc., and McCain Foods Limited.

Max Fehlmann has over 25 years of R&D management and business development experience gained within public research organizations and several biopharmaceutical companies. He has a doctorate in Biochemistry from Université Laval, a doctorate in Pharmacology from the Université de Nice and an executive MBA from the Université de Nice-Sophia Antipolis. Since March 2008, Mr. Fehlmann has been mandated to create and lead the Consortium québécois sur la découverte du medicament, an industrial consortium that brings together all of Québec’s stakeholders in drug research.

Gregory Orleski brings more than 20 years of experience in a wide variety of senior business roles to his current position as Vice-President, Business Development, Labopharm Inc and until recently, held the title of Division Counsel, Abbott Laboratories International, Pharmaceutical Products Group. Mr. Orleski received a Bachelor of Economics from the University of Alberta and then went on to obtain two law degrees from McGill University.

**CECR INTERNAL REVIEW COMMITTEE**

**Mandate**

- To ensure that the MNI’s Centre of Excellence funding decisions are consistent with goals outlined in the Federal Science and Technology Strategy.
- To ensure that funding is allocated to high priority projects and distributed in a responsible manner.
- To evaluate proposals using criteria outlined in the competitive phase of the Centres of Excellence in Commercialization and Research Program.

**Membership**

Martine Alfonso
Administrative Director, Neuroscience Mission, McGill University Health Center

Amit Bar-Or, MD
Director, Experimental Therapeutics Program and Coordinator, Clinical Research Unit, MNI

Philip Barker, PhD
Director, MNI’s Centre of Excellence in Commercialization and Research Award
Associate Director, Strategic Affairs, MNI

Robert Dunn, PhD
Associate Director, Scientific Affairs, MNI

Thomas Gevas
Chief Financial Officer, MNI

Elizabeth Kofron, PhD
Associate Director, Corporate Affairs and Special Projects, MNI

Peter McPherson, PhD
Coordinator, Cell Biology of Excitable Tissue, Neurobiology Unit, MNI

Bruce Pike, PhD
Director, McConnell Brain Imaging Centre, MNI

Eric Shoubridge, PhD
Director, Molecular Neurogenetics, MNI

David Sinclair, MD
Neurosurgeon, The Neuro

**CECR COMMERCIALIZATION COMMITTEE**

**Mandate**

- To review and advise on all potential commercial activities and will be charged with identifying the most promising technologies, with providing input into intellectual property protection and developing commercialization strategies.
- To ensure that projects with commercial potential/aspect are provided the necessary tools/ aids to avert failure.

**Membership**

Philip Barker, PhD
Director, MNI’s Centre of Excellence in Commercialization and Research Award
Associate Director, Strategic Affairs, MNI

Thomas Gevas
Chief Financial Officer, MNI

Timothé Huot, L.L.L.
Lawyer, BCF

Donald Olds, MSc, MBA
Chief Financial Officer & Chief Operations Officer, Aegera Therapeutics Inc.

Emma Saffman, PhD
Patent Agent, Ogilvy Renault

Michael Steen, PhD
Officer, Life Sciences, Office of Technology Transfer, McGill University

Patrick Tremblay, PhD
Executive-in-Residence, Pappas Ventures
We would like to thank the faculty and staff of the MNI for contributing their time in presenting their research projects and results. We would also like to acknowledge the work of photographer Owen Egan. A special thank-you to Angela Broccoli for all her help in coordinating the production of this report.

To obtain additional copies of this report or for more information, please contact:

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Montreal Neurological Institute and Hospital
3801 University Street
Montreal, Quebec H3A 2B4

External Affairs:
Tel: 514 398-1902
Fax: 514 398-8072

Communications.mni@mcgill.ca
www.mni.mcgill.ca

Le rapport est disponible en français.