HEALTHY BRAINS FOR HEALTHY LIVES

Town Hall
January 30, 2017

Rose Goldstein, Vice-Principal (Research and Innovation)

Our Vision and Goals

- Within 10 years, transform many brain disorders from terminal or life-long afflictions to treatable, or even curable, conditions.
- Reduce the human and socio-economic burden of psychiatric and neurological illnesses.
- Improve the mental health, quality of life, and productivity of people around the world.

Overall 7-year budget plan

In millions $

[redacted]		
Research (direct costs)	64.8	9.5
[redacted]		
Indirect cost	14.1	5.0
[redacted]		

Healthy Brains for Healthy Lives

$84M

AI and the Brain

Brain research and Training CIFAR

CFREF

IVADO: Artificial Intelligence/Machine Learning

Université de Montréal

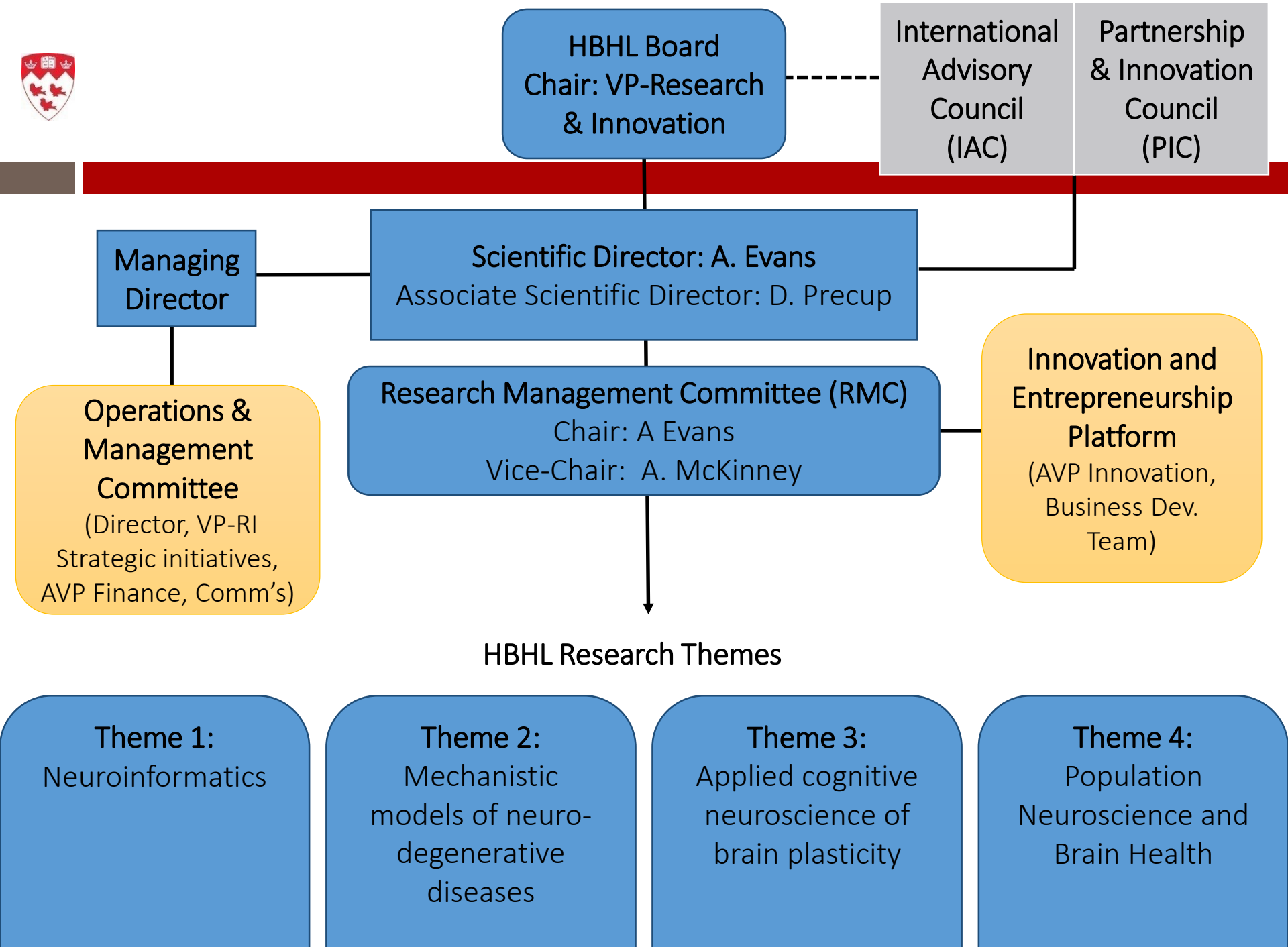
$93M

BrainsCAN

$66M

Implementation milestones

- Sep-Dec 2016 : Governance
- Feb 2017: Funding Agreement with federal government
- Winter: HBHL program development & Fund distribution
- Winter: Thematic workshops
- Winter: HBHL Admin office


HBHL Board
Chair: VP-Research & Innovation
International Advisory Council (IAC)
Partnership & Innovation Council (PIC)
Managing Director
Scientific Director: A. Evans
Associate Scientific Director: D. Precup
Operations & Management Committee
(Director, VP-RI Strategic initiatives, AVP Finance, Comm's)
Research Management Committee (RMC)
Chair: A Evans
Vice-Chair: A. McKinney
Innovation and Entrepreneurship Platform
(AVP Innovation, Business Dev. Team)
HBHL Research Themes
Theme 1:
Neuroinformatics
Theme 2:
Mechanistic models of neuro-degenerative diseases
Theme 3:
Applied cognitive neuroscience of brain plasticity
Theme 4:
Population Neuroscience and Brain Health

Key governance bodies

- Board
- Research Management Committee
- International Advisory Council
- Partnership and Innovation Council

HBHL Board

- Oversight of HBHL
- Resource allocation fair/transparent
- Expenditures aligned with HBHL goals
- Appropriate governance, management and personnel structures, policies, procedures and strategies

- Rose Goldstein (Chair)
- Christopher Manfredi
- Yves Beauchamp
- David Eidelman
- Antonia Maioni
- Bruce Lennox
- Alan Evans (Non-voting)
- Guy Rouleau (Non-voting)
- John Capone, VPR Western (External)
- 2-4 members at large

Scientific Leadership

- Scientific oversight
- Planning of research activities
- Implementation of research programs
- Delivery of HBHL mandate

Alan Evans
Scientific Director

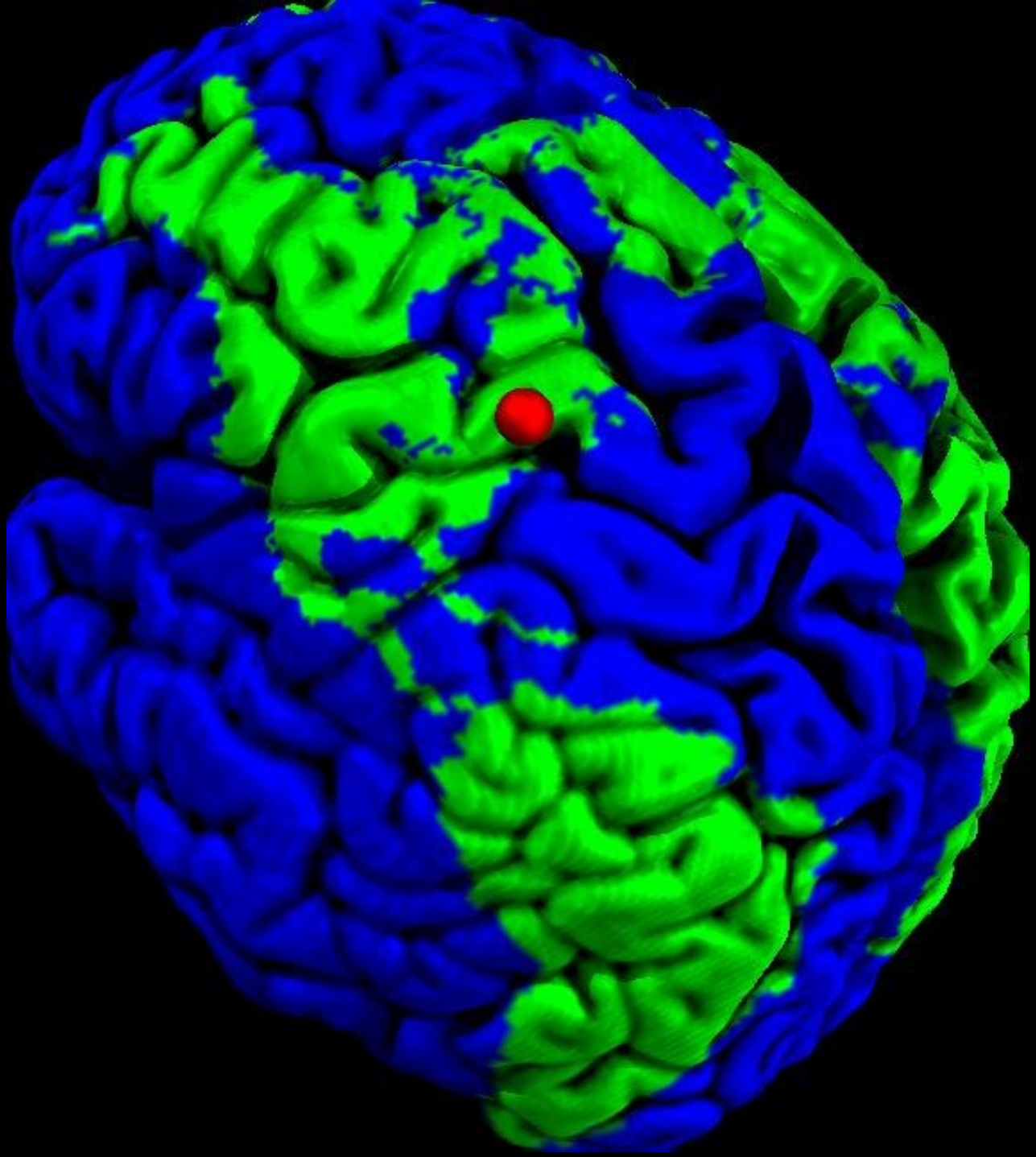
Doina Precup
Associate Scientific Director

For more information:

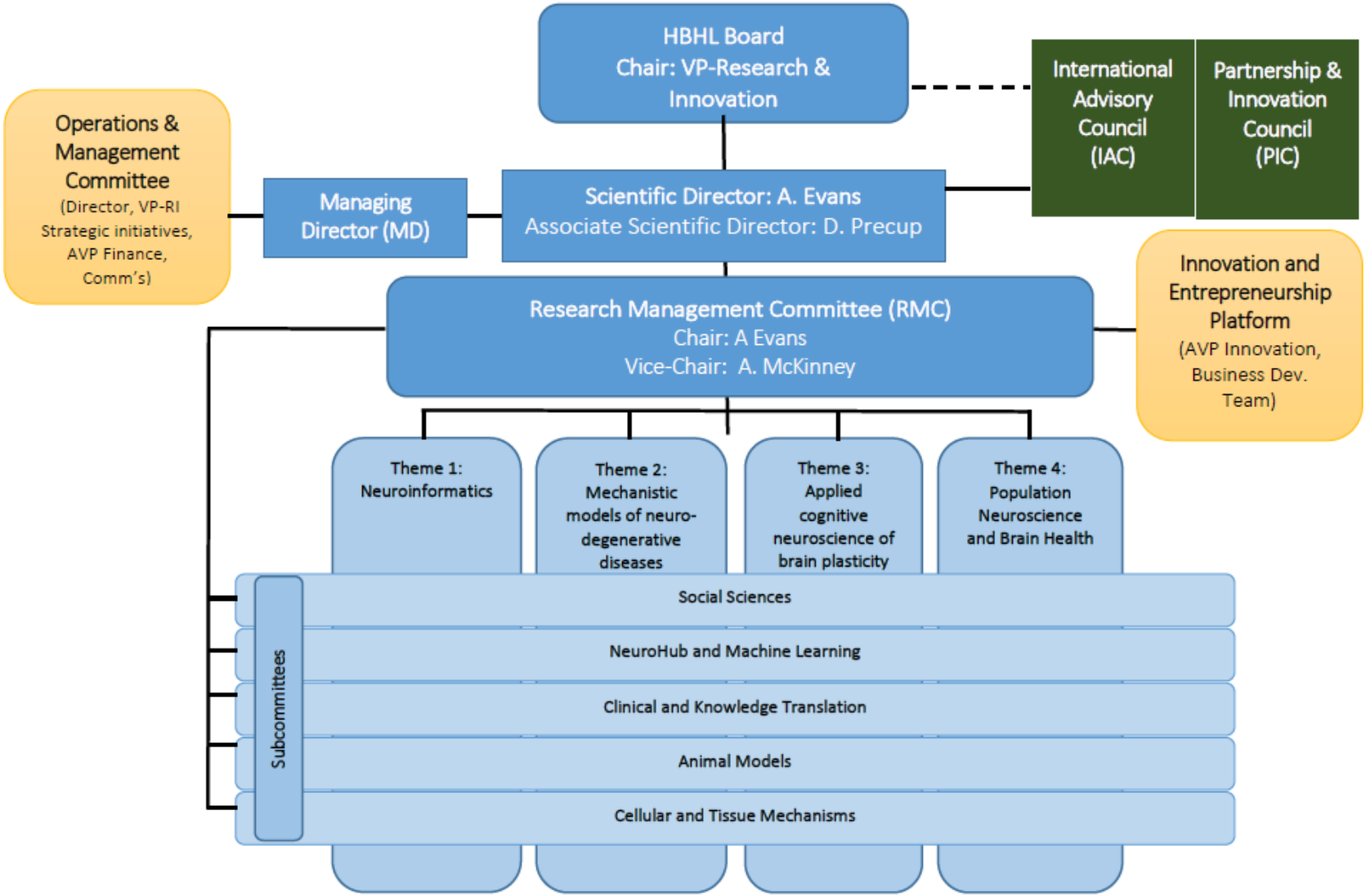
Questions?

www.mcgill.ca/hbhl

hbhl@mcgill.ca



Governance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Theme 1: Neuroinformatics
Theme 2: Mechanistic models of neuro-degenerative diseases
Theme 3: Applied cognitive neuroscience of brain plasticity
Theme 4: Population Neuroscience and Brain Health
Subcommittees
Social Sciences
NeuroHub and Machine Learning
Clinical and Knowledge Translation
Animal Models
Cellular and Tissue Mechanisms

HBHL Sub-committees

- Functions that cut across the four themes
- Tasks/tools/mechanisms supporting HBHL deliverables
- Promote interdisciplinarity

Laurence Kirmayer
Social Sciences

Doina Precup
Neurohub

Lesley Fellows

Gustavo Turecki

Clinical and Knowledge Translation

Brigitte Kieffer
Animal Models

Edward Fon
Cell and Tissue Mechanisms

Research Management Committee

- Research activities
- Advise on all aspects of HBHL
- Scientific leadership
- Resource allocation

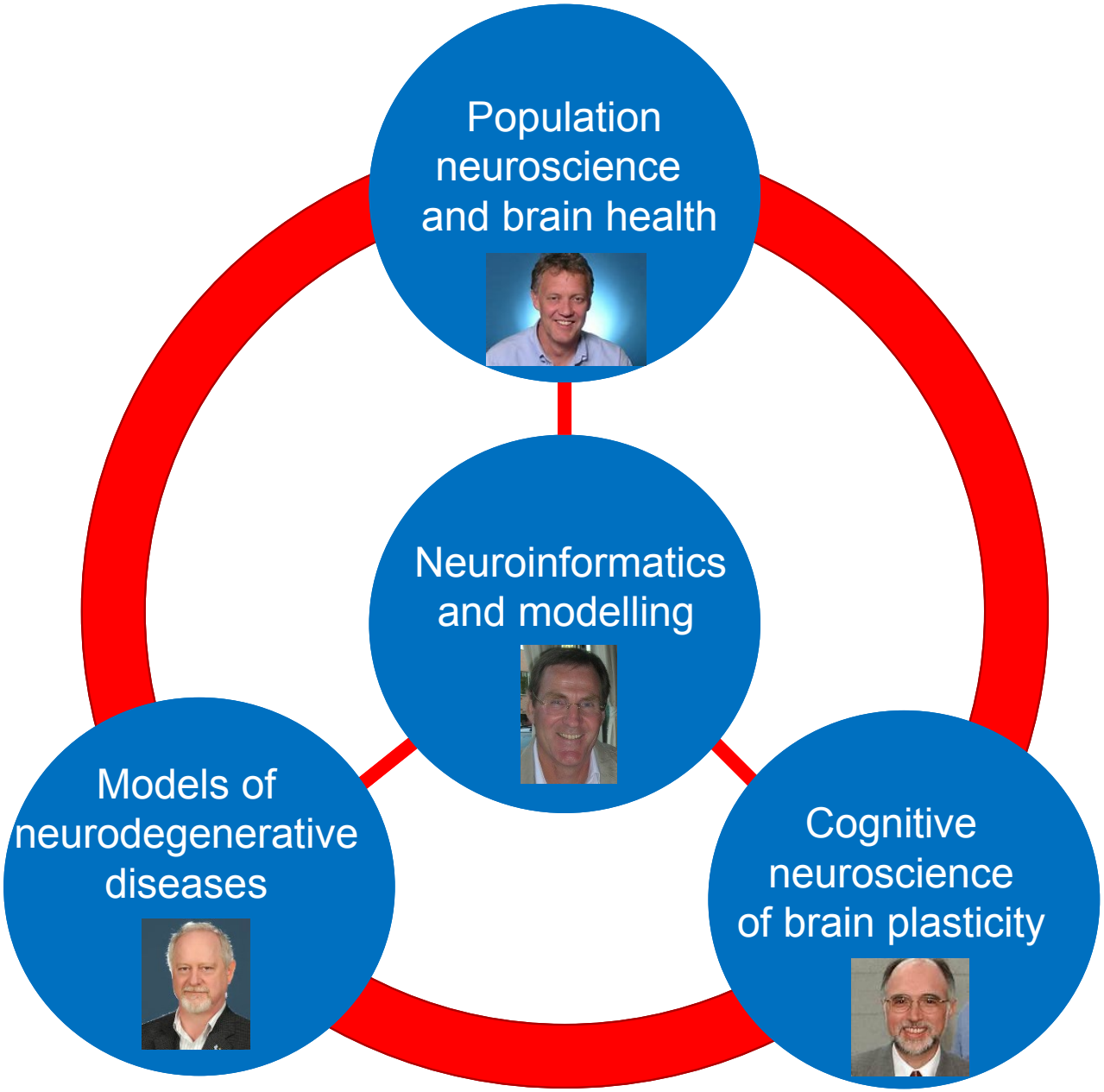
- Alan Evans (Chair)
- Anne McKinney (Vice-Chair)
- Doina Precup
- Guy Rouleau
- Brigitte Kieffer
- Laurence Kirmayer
- Robert Zatorre
- Michael Meaney
- Gustavo Turecki
- Lesley Fellows
- Ted Fon
- Julien Doyon (UdeM)
- Ravi Menon (Western)

HBHL Approach & Deliverables

- Understand the **individual** brain
- Integrate genetic, epigenetic, physiological, imaging, behavioral, environmental, clinical and social aspects
- NeuroHub - Advanced analytic platform for brain data
- By 2022: Canadian Framework for Brain Health

Healthy Brains for Healthy Lives

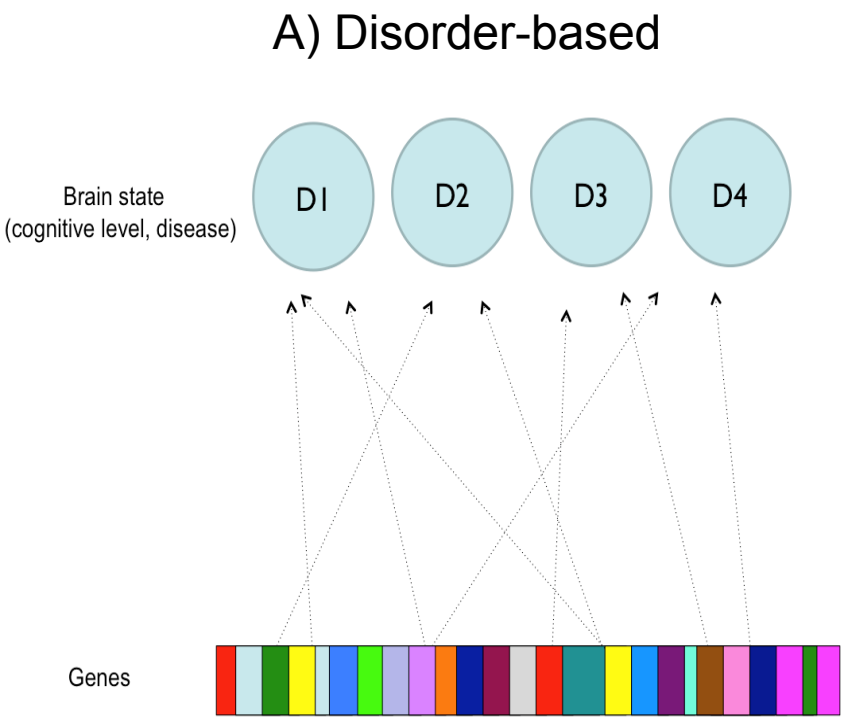
Canada First Research Excellence Fund (CFREF)

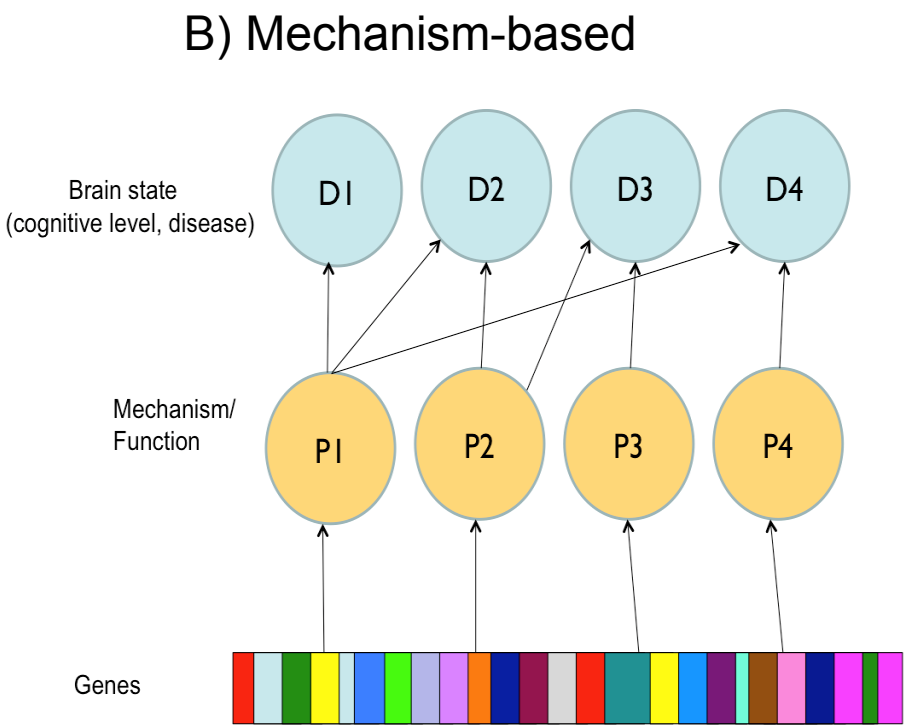


HBHL Theme 1

Neuroinformatics and Modelling

Mechanisms and circuits





A) Rather than link a gene (or genes) with a multi-factorial syndrome
B) Link genes to specific mechanisms/circuits that can be targeted and modified

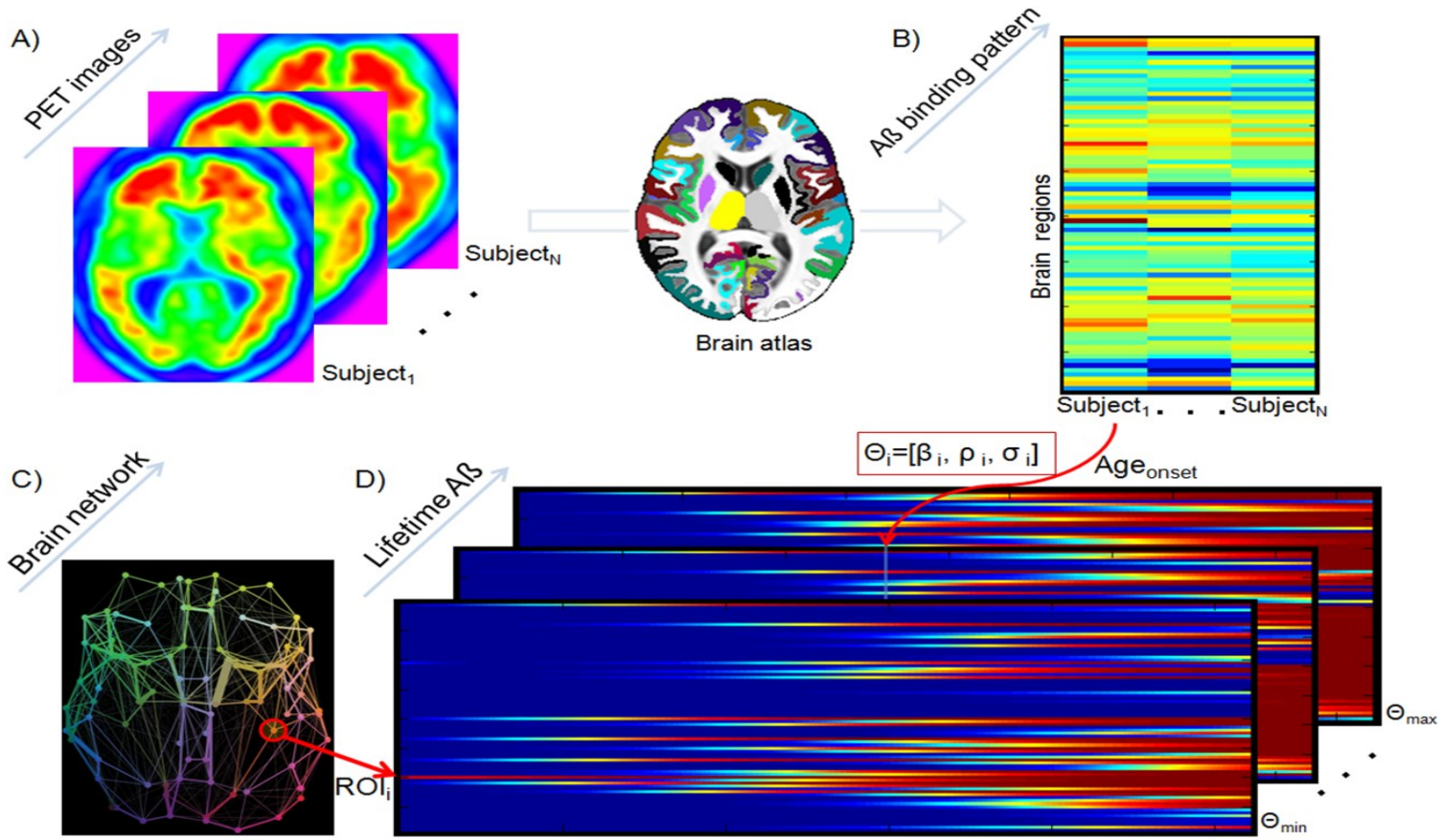
Animal model: Powerful way to decipher causes of gene-syndrome association

HBHL Theme 2

Mechanistic Models of
Neurodegenerative Disease

Epidemic Spreading Model (ESM) of $A_ß$ propagation

(**A**) measure $A_ß$ deposition pattern (**B**). Normal anatomical connectivity (**C**) is used to generate multiple hypothetical lifetime $A_ß$ propagation/deposition courses (**D**). Each hypothetical course corresponds to a set *i* of seed ROIs and model parameters θ_i,= [βi, δi, σ_i].



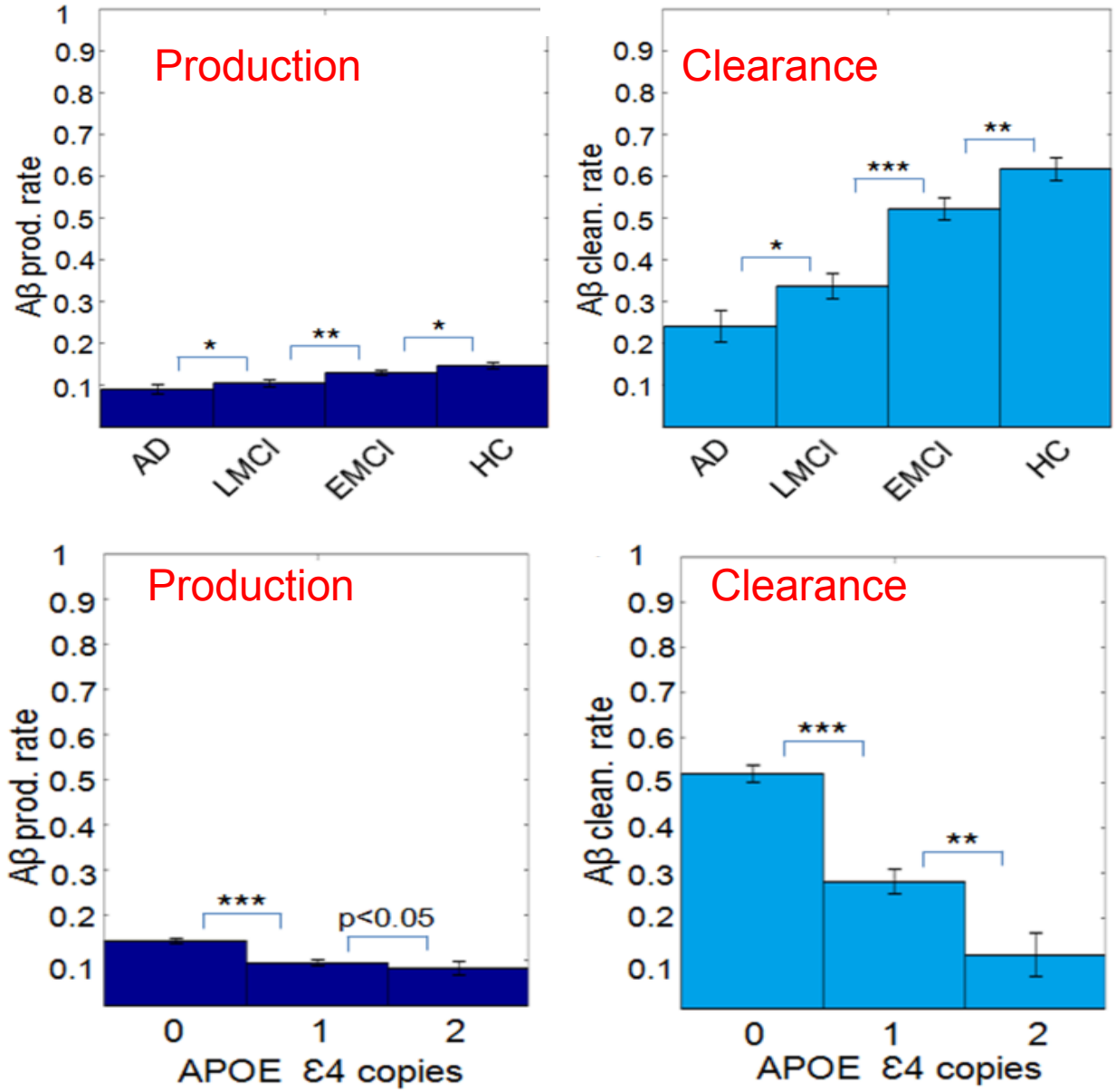
ESM iteratively estimates, per subject, the θ_i that maximizes similarity between estimated and observed $A_ß$ deposition pattern. ESM also models onset age of $A_ß$ binding and propagation.

Iturria-Medina Y, Sotero RC, Toussaint PJ, Evans AC, ADNI PLoS Comput Biol (2014)

A_β Production and Clearance Rates from ESM model

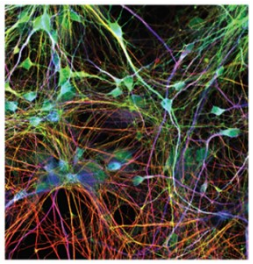
Clinical group

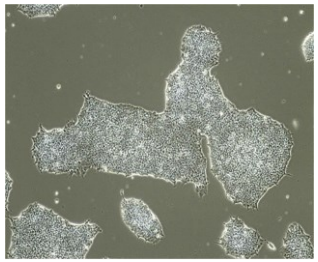
APOE ε4 alleles

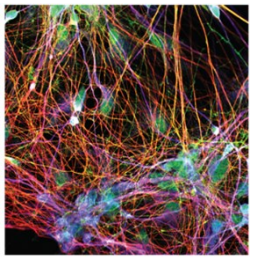


Iturria-Medina Y, Sotero RC, Toussaint PJ, Evans AC, ADNI PLoS Comput Biol (2014)

MNI Open Science
Drug Discovery Program







Problem:

Basic mechanisms of brain disease are complex and poorly understood.

Access to tissue is limited.

Not clear what new drugs should target > widespread testing, high failure rate.

Closed, proprietary approach create redundancy. Many centres test same compound.

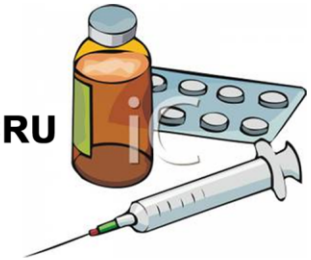
Solution:

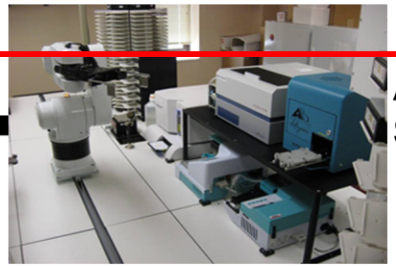
Working with human tissue/neurons is the next stage in drug discovery

"*Stem cells*" make this possible.

Disease modelling in a dish
"*Precision-Personalized medicine*"

Drug Development
Clinical trials: MNI CRU



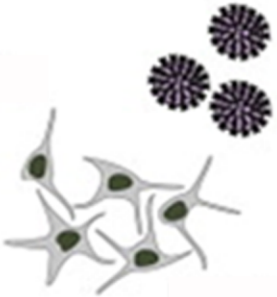


Assay development
Small molecule screening

NeurO C-BIGR
Neuro OpenScience
Clinical Biologic Imaging and
Genetic Repository

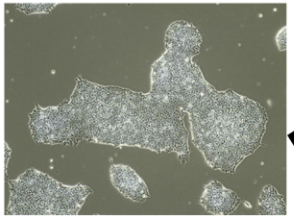
Patient

- Parkinson'sDIsease
- ALS
- Multiple Sclerosis
- Leukodystrophies
- Intellectual disabilities

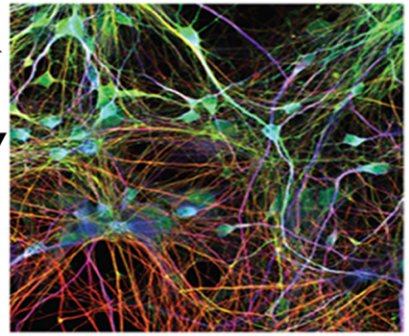


Patient Samples:
- Blood and skin cells
- Genetic data
- Imaging data
- Clinical data

iPSCs



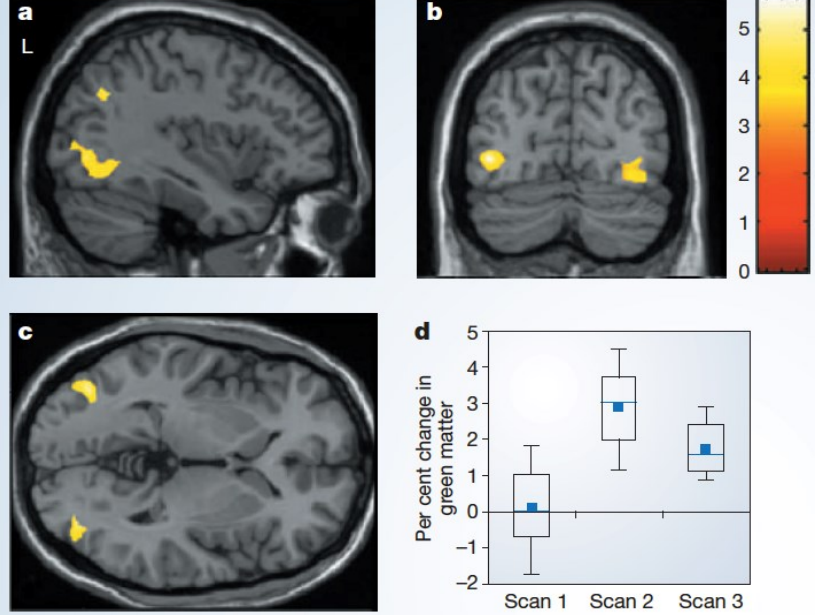
Neurons



CRISPR-Genome editing
- Correction of disease mutations
- Introduction of disease associated mutation

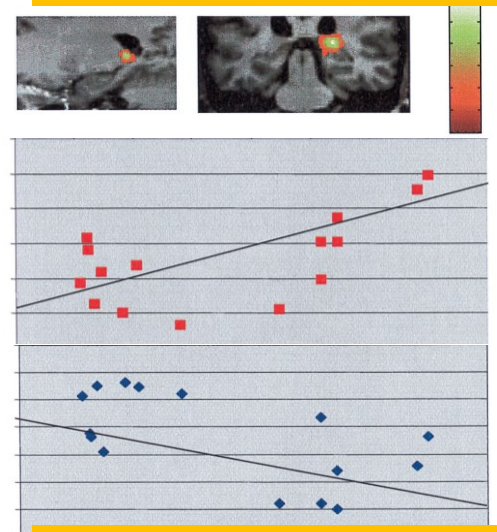
HBHL Theme 3

Applied Cognitive Neuroscience
of Brain Plasticity



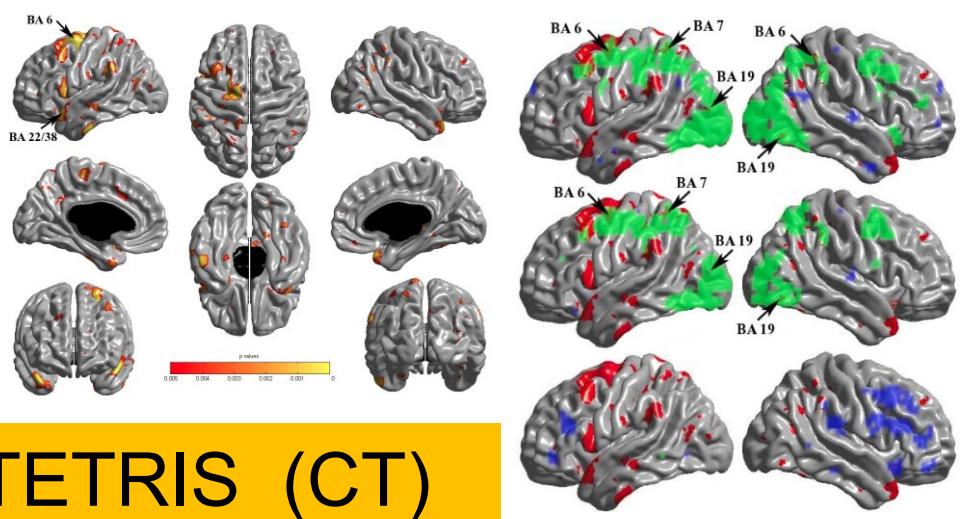
Juggling (VBM)

Draganski et al (2004)
Nature 427(6972): 311–2



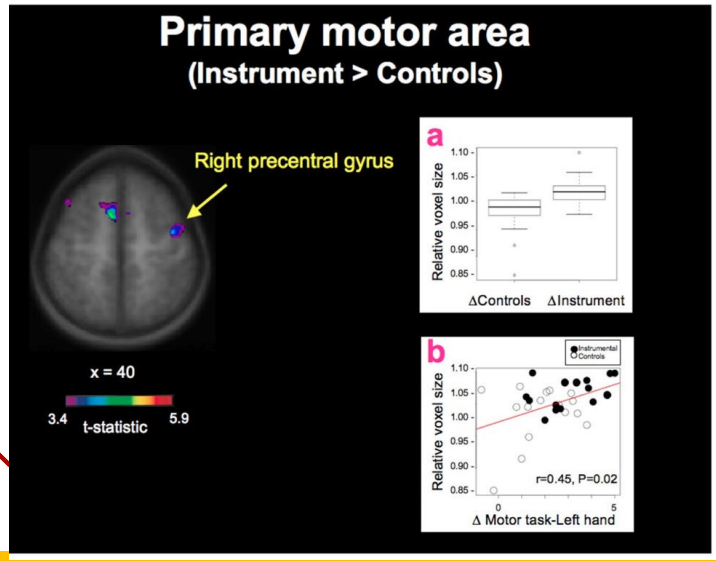
Maguire et al (2000) PNAS 97(8): 4398–4403

Cortical plasticity



TETRIS (CT)

Haier et al. (2009) BMC Res Not



Musicianship (DBM)

Hyde et al. (2009) J Neurosci 29(10): 3019-25

Navigation (VBM)

HBHL Theme 4

Population Neuroscience and Brain Health

- Neuroscience - Social Science - Population Mental Health

Social determinants of brain health

- **Workshop:** Capturing “Context”: Refining the sciences of Mind, Brain and Culture by including the Social environment

- Panel of social indicators, integrated in HBHL online platforms

- Examples of emerging projects
  - effects of migration and urban environments on mental health
  - mediators of mental health effects of microaggression and discrimination
  - interaction of social, developmental and neurobiological determinants of suicide, depression and dysphoria among Indigenous youth

Centre de ressources multiculturelles EN SANTÉ MENTALE

Multicultural MENTAL HEALTH Resource Centre

English Français

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Welcome to the MMHRC

Responding to Cultural Diversity in Mental Health

The MMHRC provides resources to support culturally safe and competent mental health care for Canada's diverse population.
Please join us to build a community of practice.

Join Our Listserv

Recent Posts

- MHCC Report: Supporting the Mental Health of Refugees to Canada
- Culture, context and mental health of Somali refugees
- Woori Maum: Korean Canadian Mental Health Association
- Catalyst – October 2016 – Case for Diversity Paints Opportunity for Service Improvement | Mental Health Commission of Canada
- The European Psychiatric Association Guidelines on Cultural Competency – Summary
- Here's Why Black People in Canada Are Healthier Than Those in the U.S. | TakePart
- Improving Cultural Competence to Reduce Health Disparities

New in the Literature

- Medical Student Mental Health: Culture, Environment, and the Need for Change.
- Individual and culture-level components of survey response styles: A multi-level analysis using cultural models of selfhood.
- Determinants of subjective well-being in people with psychosis referred for psychological therapy in South London.
- Stigma, explanatory models and unmet needs of caregivers of children with developmental disorders in a low-income African country: a cross-sectional facility-based survey.
- Developing family interventions for adolescent HIV prevention in South Africa.

Upcoming Events

Refugee Mental Health Course: Focus on Syrian Refugees
January 18 - February 14

Webinar: Group therapy programs for Syrian refugees
January 25 @ 1:00 PM - 2:00 PM

Promoting Healthy Relationships for Youth
February 15 - February 17

Action Table: Improving Mental Health Service Planning for IRER Populations
March 28 @ 8:30 AM - March 29 @ 4:30 PM

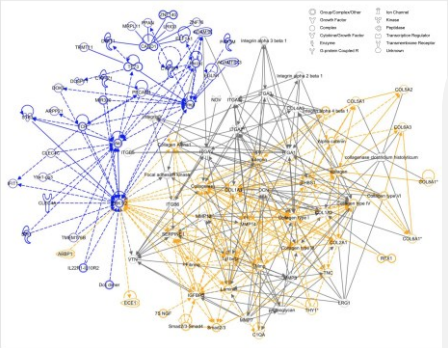
Society for the Study of Psychiatry and Culture, Annual Meeting: "Family Matters"
April 27 - April 29

View All Events

Translate Site

Select Language

HBHL Platform
Animal Models



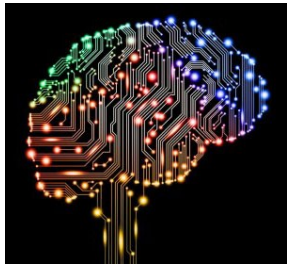
Genes & Molecular pathways

Brain Circuits

Neuroinformatics

Phenotype

Manipulate endogenous systems
Test therapeutic interventions



Measure causal effects on behaviour

Neurological disorders (Theme 2)
Development & Environment (Theme 3)
Psychiatric disorders (Theme 4)

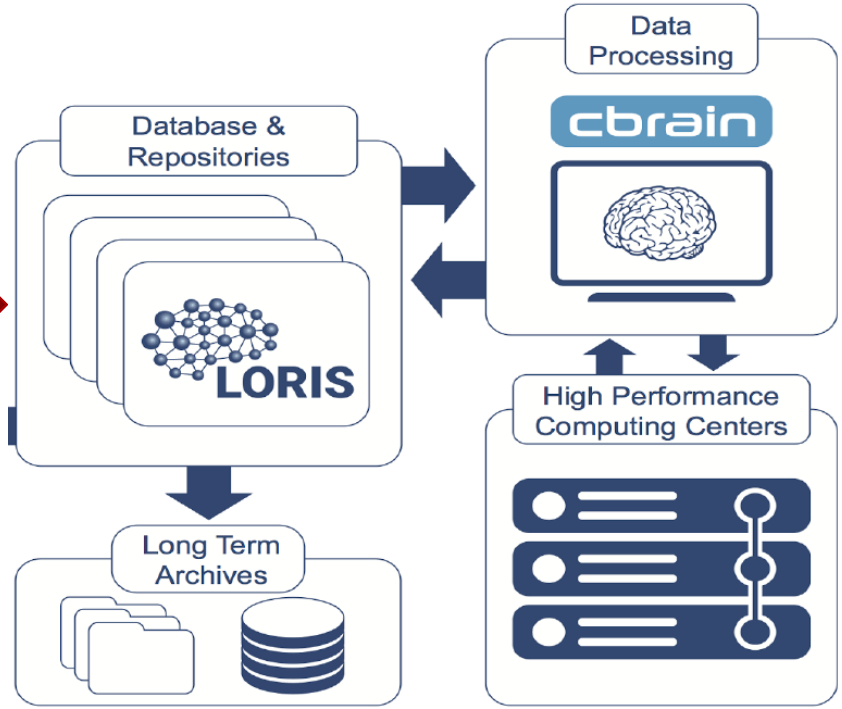
Emphasis on COGNITION
Cuts across themes
Synergy with Western U

HBHL Platform
Animal Models

Animal data

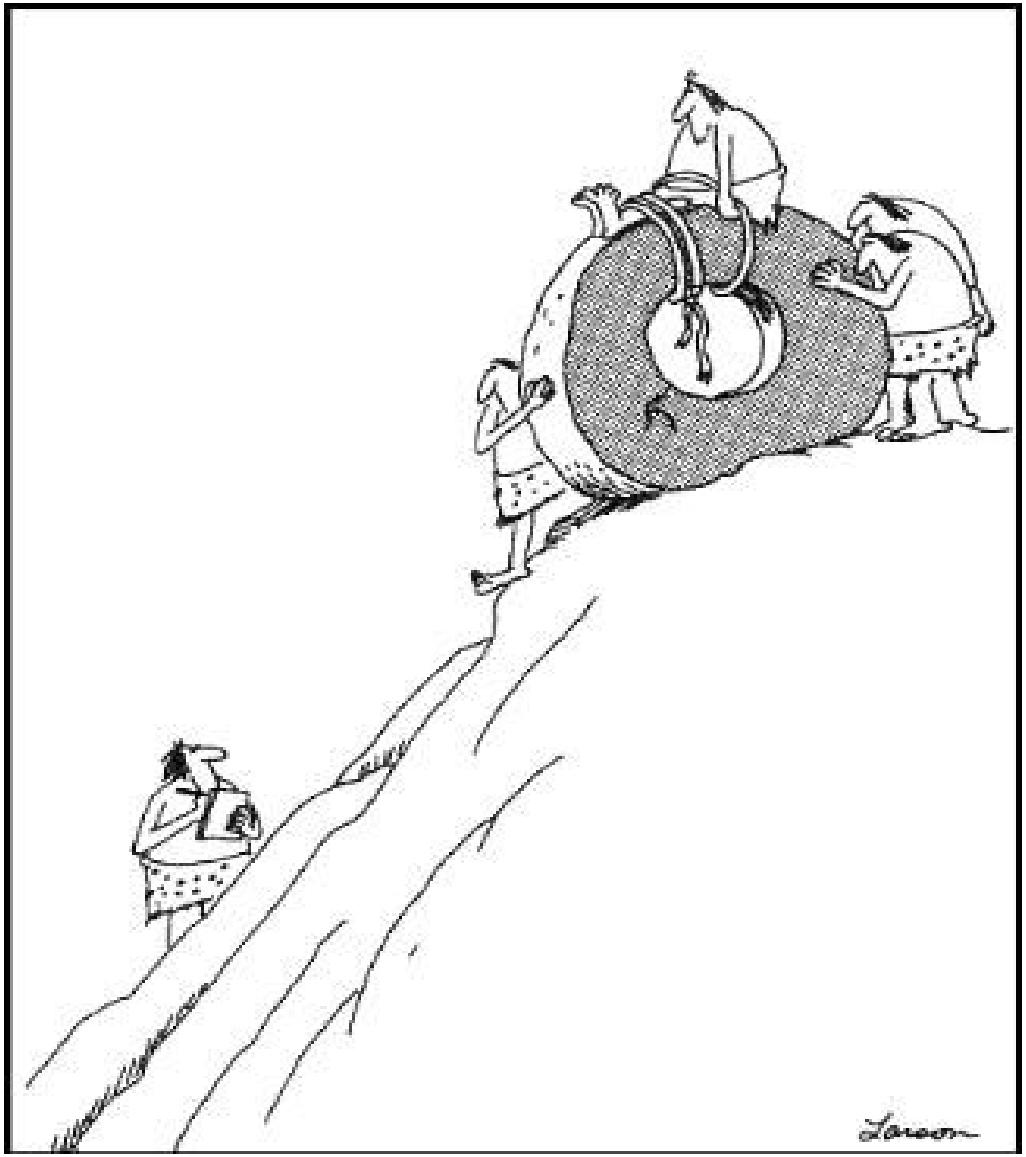
-Invasive: optogenetics & Ca imaging
-Invasive & translatable: DBS
-Non-invasive & translatable: MRI
-Behavioral phenotyping
-Deep learning & prediction
-longitudinal
-heterogeneity
-big data

Theme 1



HBHL Platform

NeuroHub



CBRAIN National HPC Integration (200,000 processors)

Canadian Consortium on Neurodegeneration in Aging,
The Canadian Component of CIHR's International Collaborative Research Strategy for Alzheimer's Disease.

compute • calcul CANADA

TOP500 SUPERCOMPUTER SITES

canarie

JÜLICH

JUROPA & JUDGE – Julich, GER
(30000 cores)

Colosse - CLUMEQ
(7616 cores)

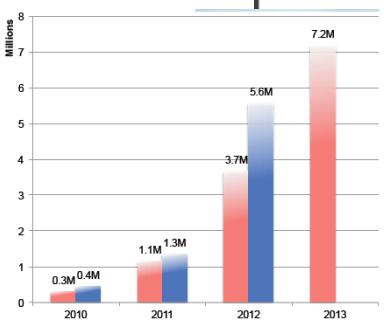
Orcinus - Westgrid
(3072 cores)

Mammouth II - RQCHP
(2464 cores)

Kraken - SHARCNET
(3774 cores)

GPC - SciNET
(30240 cores)

Guillimin - CLUMEQ & Local Servers
(16000 cores)



Data Types

Imaging
Behaviour
Genetics
Epigenetics
Tissue samples

Methods

LORIS' Genomic Browser embeds display and download tools for multiple formats of analyzed genomic data, facilitating large-scale data acquisition, dissemination and analysis in imaging-genetics research. Any format of derived genetic datasets, including metadata about genetic data collection and analysis, can be loaded and seamlessly linked with multi-modal subject data in LORIS.

Genetic/ Epigenetic

Clinical/Behavioural

Imaging

Datasets
PLINK format
Methylation CpG beta-values
Variant Analysis
GWAS, EWAS
CNV, SNP

Datasets
3D/4D including
- MRI
- MEG
- PET
- Spectroscopy

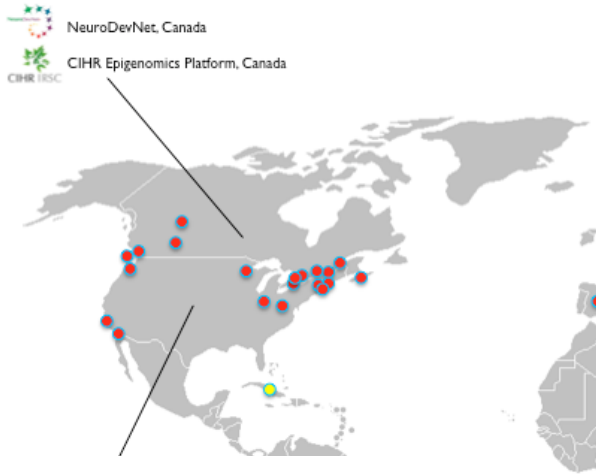
BrainBrowser[13]
Embedded Volume and Surface Viewer

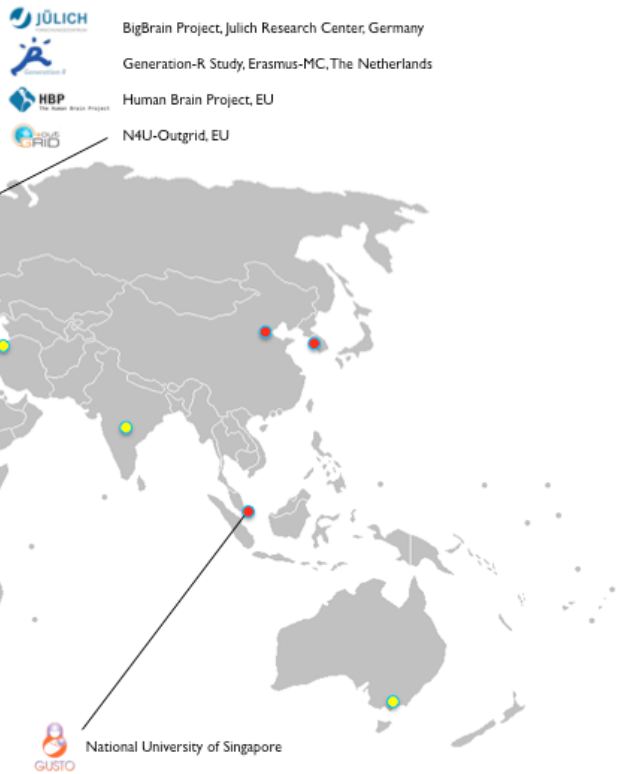
Visualization
Links to resources:
- UCSC Genome Browser[7]
- IHEC[1] Data tools
- AspireDB[11] browser

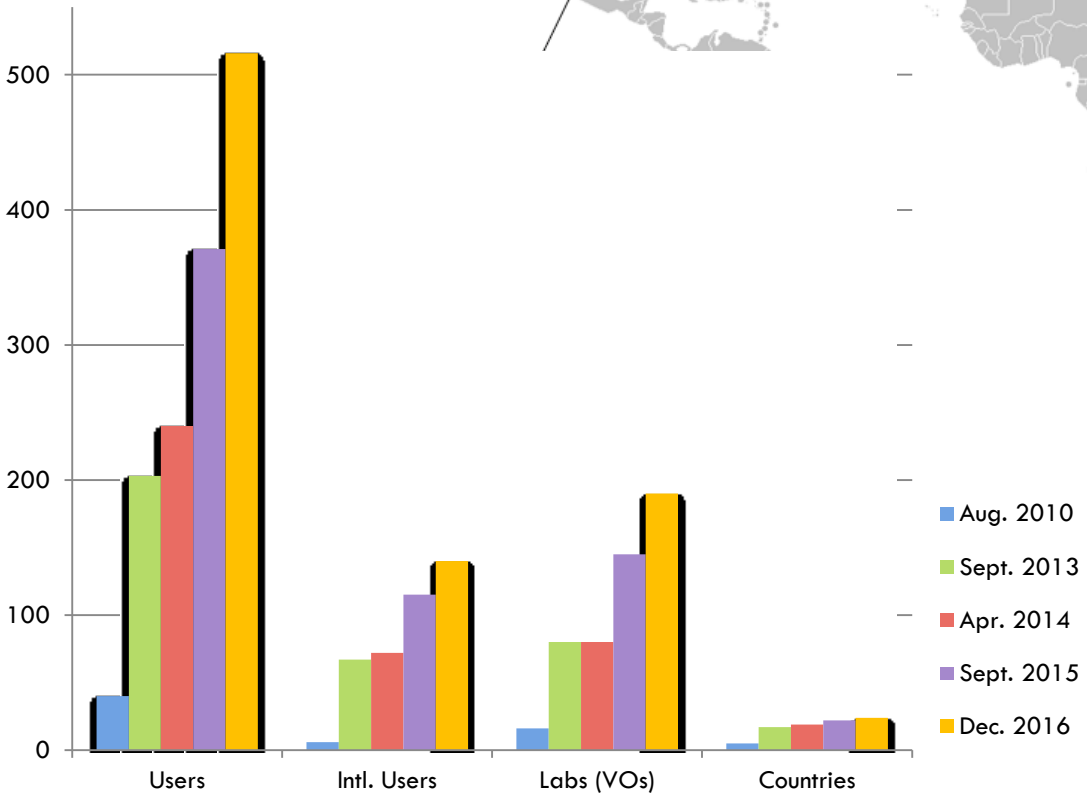
Querying
Filterable and exportable subject-based genomic profiles

Dissemination
Exporting population datasets for processing and analysis[7,10]

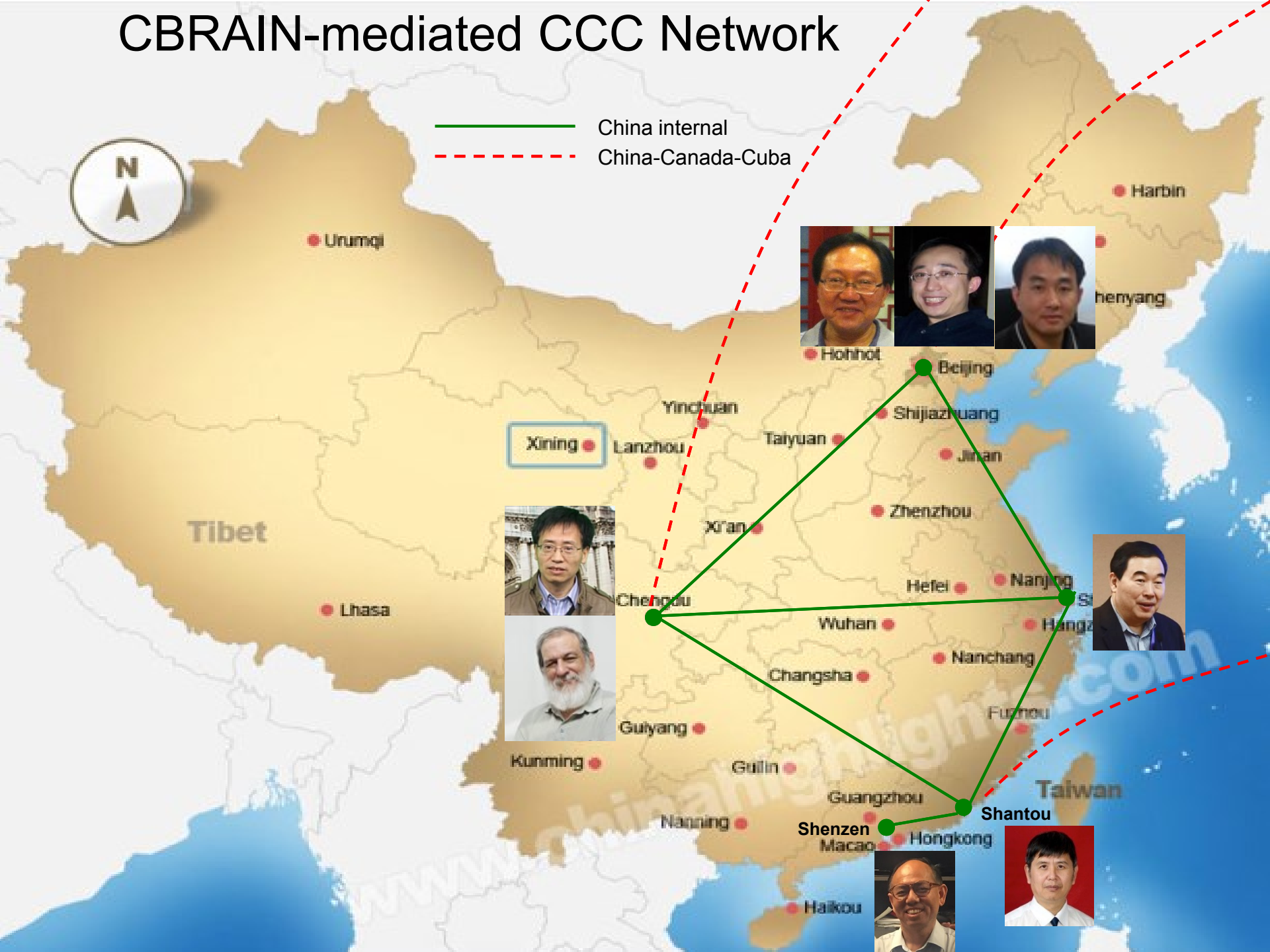
CBRAIN User Distribution





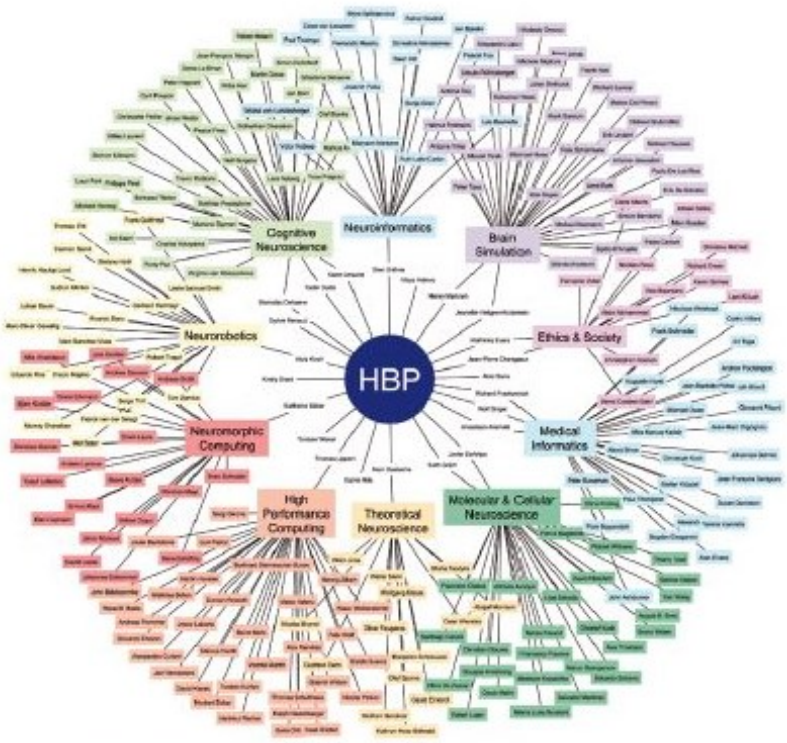


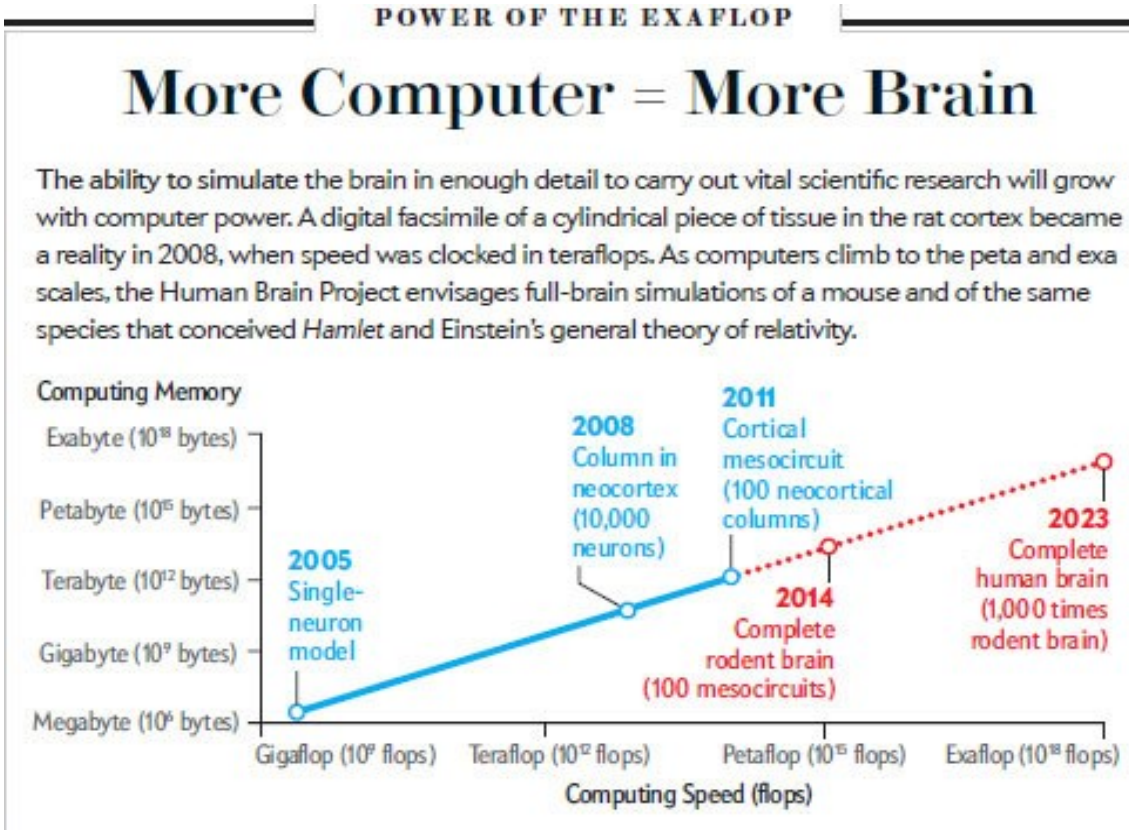
CBRAIN-mediated CCC Network




HBP
The Human Brain Project
The Human Brain Project
Launching a Human Brain Project as a FET Flagship
A Report to the European Commission


HBP
The Human Brain Project
www.humanbrainproject.eu


HBP
Cognitive Neuroscience
Neuroinformatics
Brain Simulation
Neurorobotics
Ethics & Society
Neuromorphic Computing
Medical Informatics
High Performance Computing
Theoretical Neuroscience
Molecular & Cellular Neuroscience


POWER OF THE EXAFLOP
More Computer = More Brain
The ability to simulate the brain in enough detail to carry out vital scientific research will grow with computer power. A digital facsimile of a cylindrical piece of tissue in the rat cortex became a reality in 2008, when speed was clocked in teraflops. As computers climb to the peta and exa scales, the Human Brain Project envisages full-brain simulations of a mouse and of the same species that conceived *Hamlet* and Einstein's general theory of relativity.
Computing Memory
Exabyte (10^{18} bytes)
Petabyte (10^{15} bytes)
Terabyte (10^{12} bytes)
Gigabyte (10^{9} bytes)
Megabyte (10^{6} bytes)
2005 Single-neuron model
2008 Column in neocortex (10,000 neurons)
2011 Cortical mesocircuit (100 neocortical columns)
2014 Complete rodent brain (100 mesocircuits)
2023 Complete human brain (1,000 times rodent brain)
Gigaflop (10^{9} flops)
Teraflop (10^{12} flops)
Petaflop (10^{15} flops)
Exaflop (10^{18} flops)
Computing Speed (flops)

THE WHITE HOUSE IS ANNOUNCING
OVER $300 MILLION IN PUBLIC AND PRIVATE INVESTMENTS IN SUPPORT OF THE BRAIN INITIATIVE

the WHITE HOUSE

BRAIN INITIATIVE

BRAIN RESEARCH THROUGH ADVANCING INNOVATIVE NEUROTECHNOLOGIES

Since President Obama announced the **BRAIN Initiative** in April 2013, dozens of leading technology firms, academic institutions, scientists and other key contributors to the field of neuroscience have answered his call and made significant commitments to advancing the Initiative.

Building off of $100 million in commitments announced last year at NIH, NSF and DARPA, the BRAIN Initiative is growing to five participating federal agencies with the addition of FDA and IARPA.

NIH
NATIONAL INSTITUTES OF HEALTH

NIH is announcing $46 million in new BRAIN-related grant awards, focusing on new tools and techniques

FDA
FOOD AND DRUG ADMINISTRATION

FDA is joining the BRAIN Initiative, with the goal to enhance the transparency of the regulatory landscape for neurological medical devices

IARPA
INTELLIGENCE ADVANCED RESEARCH PROJECTS ACTIVITY

IARPA is joining the BRAIN Initiative and will use multidisciplinary approaches to advance understanding of cognition and computation in the brain

DARPA
DEFENSE ADVANCED RESEARCH PROJECTS AGENCY

DARPA is building on four existing programs and is planning new investments in the BRAIN Initiative, with the ultimate goal of relieving and rehabilitating warfighters and civilians suffering from traumatic injury and neuro-psychiatric illness

NSF
NATIONAL SCIENCE FOUNDATION

NSF is continuing to make investments to support BRAIN Initiative by accelerating fundamental research and the development of new technologies for neuroscience and neuroengineering

PRIVATE SECTOR COMMITMENTS

$30 MILLION US PHOTONICS INDUSTRY

$5 MILLION GLAXOSMITHKLINE

GOALS

To develop new optics and photonics technologies to tackle challenges of the BRAIN Initiative

Fund innovative peripheral neurotechnologies and provide unrestricted, royalty-free access for research purposes to all intellectual property developed through this challenge

PRIVATE RESEARCH EFFORTS

$65 MILLION UNIVERSITY OF PITTSBURGH

Creating a new University of Pittsburgh Brain Institute focused on unlocking the mysteries of normal and abnormal brain function

$12 MILLION UNIVERSITY OF CALIFORNIA, BERKELEY AND CARL ZEISS MICROSCOPY

Infrastructure for neurotechnology development

$40 MILLION THE CARNEGIE MELLON UNIVERSITY

Commitment to support the goals of the BRAIN Initiative

$62 MILLION THE SIMONS FOUNDATION

To uncover patterns of the neural activity that produce cognition by combining analyses of internal mental states with studies of sensory and motor processing.

Continuing Progress from Existing Partners

$60 MILLION ANNUALLY THE ALLEN INSTITUTE FOR BRAIN SCIENCE

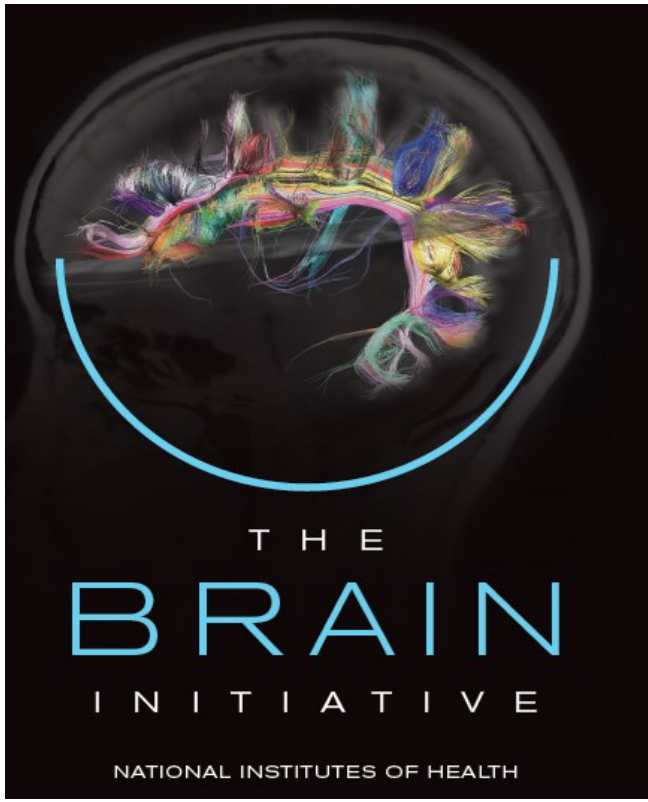
Understand how brain activity leads to perception, decision making and ultimately action

$70 MILLION HOWARD HUGHES MEDICAL INSTITUTE

Develop new imaging technologies and understand how information is stored and processed in neural networks

$40 MILLION OVER THE NEXT 10 YEARS KAVLI FOUNDATION

Provide the knowledge for addressing debilitating diseases and conditions



POSSIBLE LONG-TERM OUTCOMES

The BRAIN Initiative has the potential to do for neuroscience what the Human Genome Project did for genomics by supporting the development and application of innovative technologies that can create a dynamic understanding of brain function. It aims to help researchers uncover the mysteries of brain disorders, such as Alzheimer's and Parkinson's diseases, depression, Post-Traumatic Stress Disorder (PTSD), and traumatic brain injury (TBI).

The Human Genome Project demonstrates the potential impact that ambitious research programs like the BRAIN initiative can have.
From 1988-2003, the Federal Government invested $3.8 billion in the Human Genome Project, which has since generated an economic output of $796 billion —a return of $141 for every $1 invested.

Canadian Brain Initiative

Translational focus a Canadian strength

Large enough for global impact, small enough to be “organizable”

Mature national neuroinformatics infrastructure

Potentiate not dictate

Provide analytic infrastructure

Foster open, collaborative projects at different levels

Cross-disciplinary training and career paths

Research Programs – Direct Costs

Research ($20.4M)	Talent ($17.8M)
Discovery Fund interdisciplinary research Research Transition Awards Innovative Ideas	Student and Postdoctoral Fellowships New Investigators start-up grants Visiting Fellows
Innovation ($11.2M)	**Infrastructure ($15.4M)**
International Collaboration Platform Neuro-Innovation Fund (1:1 matched) Knowledge Mobilization	Technology Development Core facilities Operations

Research

- **Interdisciplinary Discovery Fund:** Strategic and long-term research for interdisciplinary teams :
  - Up to 400K/year x 3 year (2-4 awards per year)

- **Innovative Ideas:** Exploration of novel and innovative ideas with the potential for breakthrough science.
  - Seed ($25K x 1 year)
  - Vision ($100K x 2 years)
  - 5 per year (each)

Talent

- **Support for graduate students** (MA and PhD, 20 per year) **& Postdoctoral Fellows** (10 per year)**:** Interdisciplinary training

- **New Investigators Start-up:** for recruitment of new faculty: equipment and direct research costs ($250K-500K/HBHL hire ~3 per year)

- **Visiting Fellows:** Academic exchange. Fellowships and travel ($50K x 4 per year)

Innovation

- **International Collaboration Platform:** Respond quickly to emerging international opportunities. Link with partners. (~$500k per year, total)

- **Neuro-Innovation Fund:** Matched by Quebec Gov., in collaboration with industry and other partners (~$500k per year, total)

- **Knowledge Mobilization:** Research and Innovation Chairs, Knowledge Translation (KT) policy, products, or processes. ($100K/year, 1 year, 6 awards per year)

Infrastructure

- **Technology Development:** Specialized professionals for technology development of tools and processes e.g. programmers, statisticians, mathematicians, $400k x 3 awards per year, multi-year duration

- **Core Facilities Operations:** Operations, maintenance, upgrades, expansions of existing HBHL platforms. ~$1M per year total

Projected Rollout

Program	Launch
Theme Development Workshops ("Road map")	Dec 2016
International Collaboration	Dec 2016
Core Platforms	Dec 2016
Innovative ideas (Pilot)	Spring
Visiting Fellows (Pilot)	Spring
Technology Development (Pilot)	Spring
Student Scholarships & Fellowships	Spring
Neuro-Innovation Fund	Spring
Knowledge Mobilization	Summer
Interdisciplinary Discovery Research Teams	Summer

Questions?

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