Canadian Academy of Health Sciences
Académie canadienne des sciences de la santé

CANADA'S POSITION IN THE GLOBAL SCIENTIFIC EFFORT TO PREVENT, SLOW AND TREAT DEMENTIA

DR. HOWARD CHERTKOW

PROFESSOR OF NEUROLOGY

MCGILL UNIVERSITY

Disclosures

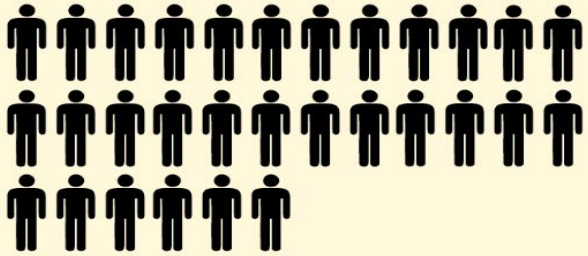
Dr. Chertkow is PI for clinical trials in Alzheimer Disease for Roche, TauRx, Merck, Abbvie, and Servier.

Past: Adjudication board for Bristol Myers Squibb

No other disclosures

Canadians living with Alzheimer and other dementias

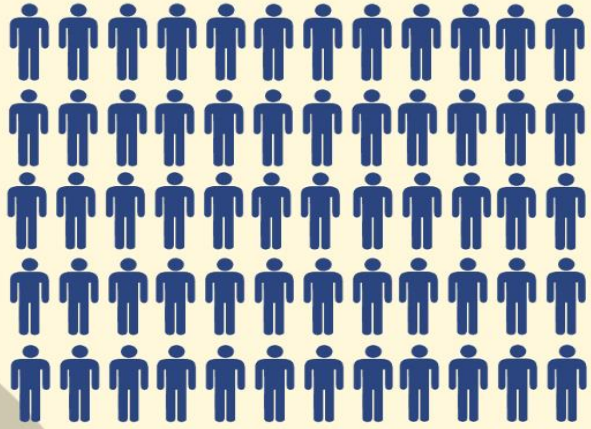
2011



x 25 000 =

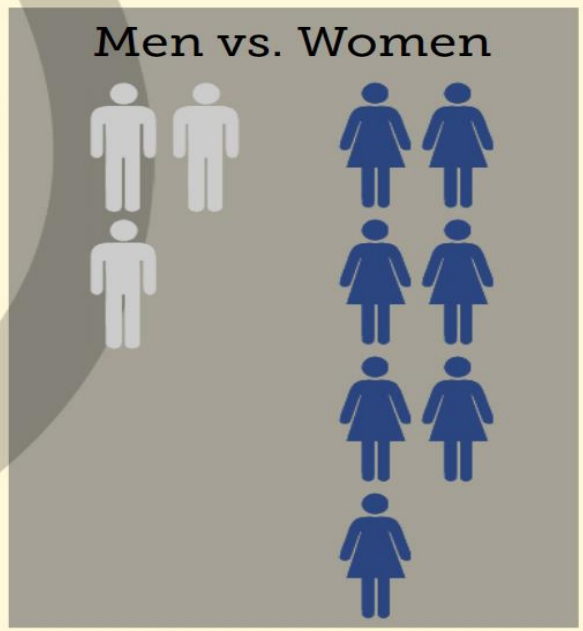
747 000

2031



x 25 000=

1.4 Million



72% Women

$214 Million

CIHR funding in dementia research over the last 10 years

Economic cost of dementia

2011

$33 Billion

2040

$293 Billion

Statistics supplied by:
Alzheimer Society of Canada

2012

CIHR Dementia Research Strategy

The CIHR Dementia Research Strategy (the Strategy) supports research on the latest preventive, diagnostic and treatment approaches to Alzheimer's disease and related dementia. It consists of an international and a national component. Together, these components allow the Government of Canada to support world-class research on dementia that will contribute to the global pursuit of finding a cure or disease-modifying treatment for dementia by 2025. The Strategy enables Canadian researchers to lead and participate in a new wave of national and international initiatives.

The goals of the Strategy fall under the following three themes:

- **Primary Prevention –** Preventing the disease from occurring through the identification of the mechanisms and/or conditions responsible for the neurodegenerative processes that lead to Alzheimer's disease and related dementias.
- **Secondary Prevention –** Delaying/slowing the clinical progression of an already developing disease though better understanding of the mechanisms, diagnosis and early intervention.
- **Quality of life –** Improving the quality of life of those living with the disease or who support those having the disease as well as to improve access to quality care and enabling the healthcare system to deal more efficiently with the rising number of individuals with dementia.

The Strategy is led by the CIHR Institute of Aging and co-led by the CIHR Institute of Neurosciences, Mental Health and Addiction.

Canadian Consortium on Neurodegeneration in Aging

- Over 350 collaborating researchers
- 20 research teams
- 8 national platforms
- 4 cross cutting components:
- Women, Sex and Gender
- Training
- Ethical, Legal and Social Implications (ELSI)
- Knowledge Transfer/Exchange

Canadian Consortium on Neurodegeneration in Aging

The Canadian Consortium on Neurodegeneration in Aging (CCNA) provides the infrastructure and support that enables collaboration amongst Canada's top dementia researchers. By accelerating discovery, innovation, and the adoption of new knowledge, the CCNA positions Canada as a global leader in increasing understanding of neurodegenerative diseases, working towards prevention, and improving the quality of life of those living with them.

CCNA – Partners

Institute of Aboriginal Peoples' Health
Institute of Aging
Institute of Circulatory and Respiratory Health
Institute of Gender and Health
Institute of Neurosciences, Mental Health and Addiction

Canadian Consortium on Neurodegeneration in Aging

Five year budget is $32 million CAN.

CROSS-CUTTING PROGRAMS

TRAINING & CAPACITY BUILDING

KNOWLEDGE TRANSFER

ELSI

WOMEN & DEMENTIA

Theme 1:
PREVENTION

1. Genetics of NDD
2. Inflammation & Growth Factors
3. Protein Misfolding
4. Synapses & Metabolomics
5. Lipids & Lipid Metabolism
6. Nutrition, Lifestyle, & Prevention of AD

Theme 2:
TREATMENT

7. Vascular Aspects of NDD
8. Lewy Body Dementia
9. Biomarkers
10. Cognitive Intervention and Brain Plasticity
11. Prevention and Treatment of Neuropsychiatric Symptoms
12. Mobility, Exercise, and Cognition
13. Frontotemporal Dementia

Theme 3:
QUALITY OF LIFE

14. How Multi-Morbidity Modifies the Risk and the Patterns of Disease
15. Gerontechnology & Dementia
16. Driving & Dementia
17. Interventions at the Sensory and Cognitive Interface
18. Effectiveness of Caregiver Intervention
19. Integrating Dementia Patient Care into the Health Care System
20. Issues in dementia care for rural and indigenous populations

Eight Platforms to Support the

1. Clinical Cohorts
2. The Normative Comparison Group
3. Imaging/Database/Information Technology
4. Blood, Saliva & CSF Biosamples
5. DNA Sequencing
6. Brain Banking
7. Transgenic Colonies
8. Academic Clinical Trials

Specific Objectives of the CCNA

• **To carry out transformative research that advances understanding of the biology, natural history, clinical presentation and management of Alzheimer disease (AD) and other neurodegenerative diseases (NDD), resulting in new and better treatment of these diseases**.

1. **ACCELERATE THE APPLICATION OF TRANSLATIONAL RESEARCH IN CLINICAL SETTINGS**: Provide a critical link between basic science research programs in NDD and clinical populations.

2. DEVELOP NEW TREATMENTS AND INTERVENTIONS.

3.CREATE A NATIONAL NETWORK OF RESEARCHERS ON NDD.

4. **ESTABLISH A NATIONAL RESEARCH INFRASTRUCTURE.**

5. **IDENTIFY AND INVEST IN NATIONAL PRIORITIES:** - service delivery challenges, care within different provincial systems., rural and indigenous communities.

6. **BUILD SYNERGY ACROSS THE BROADER NEURODEGENERATIVE DISEASE COMMUNITY:** focussing on neurodegenerative diseases beyond AD to study common mechanisms and shared pathologies.

7. CATALYZE NOVEL CLINICAL TRIALS IN DEEPLY PHENOTYPED COHORTS.

8. **ENABLE INTERNATIONAL COLLABORATIONS.**

9. LINK NDD RESEARCHERS WITH CANADIAN RESEARCH ON NORMAL AGING: - formal links between CCNA and the Canadian Longitudinal Study on Aging.

10. DEVELOP NOVEL INTERVENTIONS AVAILABLE TODAY THAT CAN IMPROVE THE CARE AND MANAGEMENT OF PEOPLE LIVING WITH NDD.

Teams - Theme 1: Basic Mechanisms & Prevention of cognitive impairment and dementia

Theme Leaders: Jane Rylett, David Hogan

Team 1 - Clinical genetics and gene discovery

Leader: Peter St. George-Hyslop (U.of T.)

Team 2 - Inflammation and Nerve Growth Factors

Leader: Claudio Cuello (McGill)

Team 3 - Protein Misfolding

Leader: Neil Cashman (UBC)

Team 4 - Synapses and metabolomics

Leader: Robert Bartha (Western)

Team 5 - Lipid and Lipoprotein Metabolism

Leader: Cheryl Wellington (UBC)

Team 6 - Nutrition, Exercise and Lifestyle in AD prevention

Leader: Carol Greenwood (U. of T.)

Teams - Theme 2: Diagnostics & Treatments

Theme Leaders: Sandra Black (U. of T.), Mario Masellis (U. of T.)

Team 7 - Vascular illness and its impact on NDD

Leaders: Eric Smith (U. Calgary), Joanne McLaurin (U. of T.)

Team 8 - Lewy Bodies (PDD and LBD), Aging, and Dementia

Leader: Richard Camicioli (U. Alberta)

Team 9 - Developing New Biomarkers

Leaders: Roger Dixon (U. Alberta), Pierre Bellec (U. de Montréal)

Team 10 - Cognitive Intervention and Brain Plasticity

Leader: Sylvie Belleville (U. de Montréal)

Team 11 - Prevention and Treatment of Neuropsychiatric Symptoms

Leaders: Nathan Herrmann (U. of T.), Krista Lanctôt (U. of T.), Dallas Seitz (Queen's)

Team 12 - Mobility, Exercise and Cognition

Leaders: Manuel Montero-Odasso (Western), Louis Bherer (Concordia)

Team 13 - Frontotemporal dementia

Leader: Robin Hsiung (UBC)

Teams- Theme 3: Disease Management & Quality of Life Leaders: Kenneth Rockwood (Dalhousie), Kathy McGilton (U. of T.)

Team 14 - How multi-morbidity modifies the risk of dementia

Leader: Melissa Andrew (Dalhousie)

Team 15 - Gerontechnology and dementia

Leader: Alex Mihailidis (U. of T.)

Team 16 - **Driving and dementia**

Leaders: Gary Naglie (U. of T.), Mark Rapoport (U. of T.)

Team 17 - Interventions at the Sensory and Cognitive Interface

Leader: Natalie Phillips (Concordia)

Team 18 - Program to improve the effectiveness of dementia caregivers

Leader: Joel Sadavoy (U. of T.)

Team 19 - Integrating dementia patient care into the health care system

Leaders: Howard Bergman (McGill), Isabelle Vedel (McGill)

Team 20 - Issues in care for rural and indigenous populations

Leaders: Debra Morgan (U. Saskatchewan), Kristen Jacklin (Northern Ontario School of Medicine), Carrie Bourassa (First Nations University).

Teams in red are in social/health services domains

The CCNA national patient cohorts

Recruiting 1600 subjects with various neurodegenerative disease conditions, via sites at academic Memory Clinics, Stroke Clinics, and Movement Disorders clinics

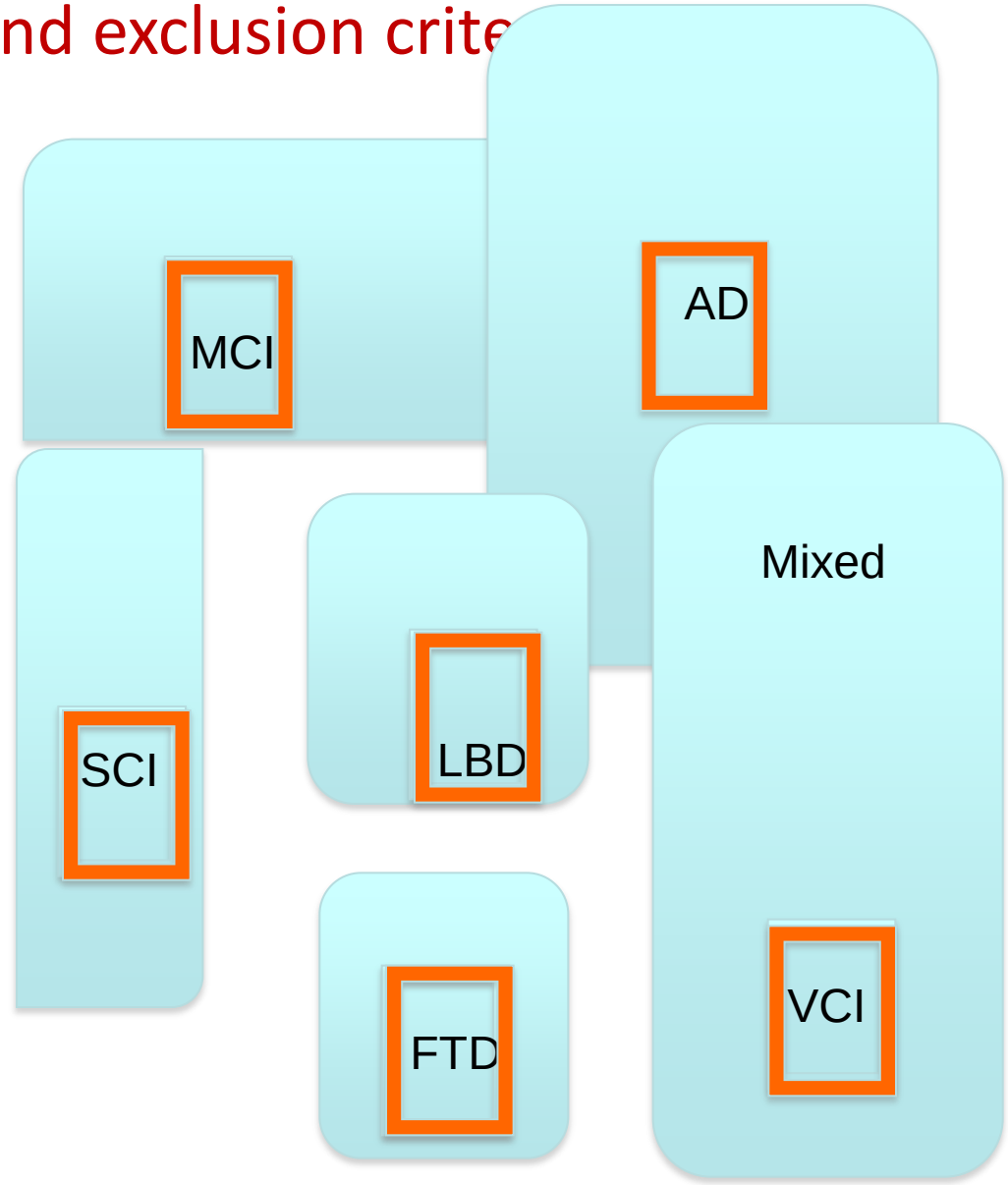
Diagnosis	Minimum Number
Subjective Cognitive Impairment	200
Mild AD	200
Mixed AD/Vascular Dementia/VCI -Vascular Cognitive Impairment	400
Mild Cognitive Impairment	400
Lewy Body Disease/ Parkinsons Dementia	200
Frontal temporal dementia	200

Choice of Inclusion and exclusion crite

If narrowly-focussed criteria, will produce homogeneous groups that represent a small fraction of the dementia population.

May exclude co-morbidities and mixed dementias

ADNI example

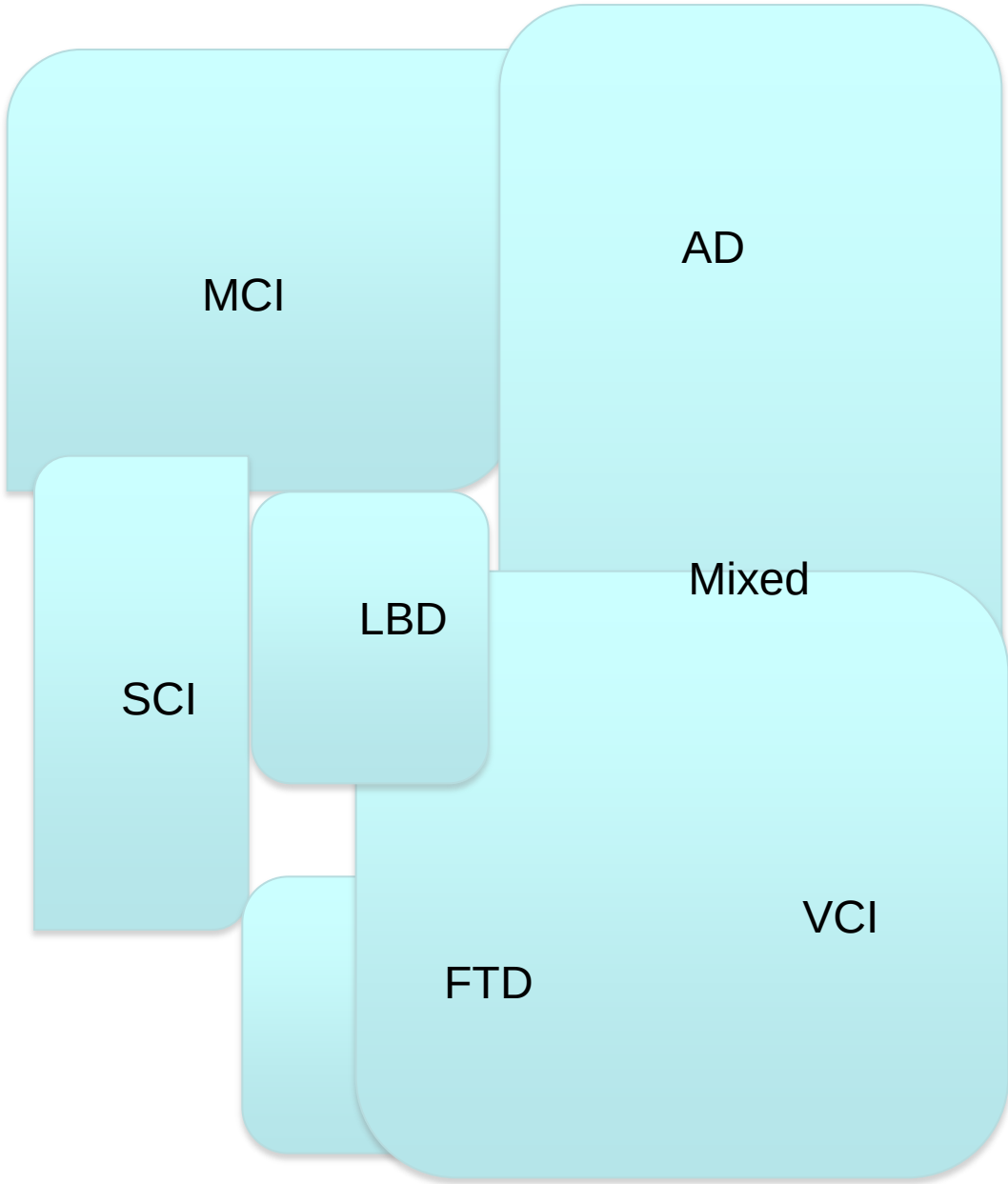


Choice of Inclusion and Exclusion criteria

Broadly inclusive criteria will produce heterogeneous groups that cover the entire dementia population.

Include almost all co-morbidities and mixed dementias

Difficult to specify definitions of “pure” disease



Choice of Inclusion and Exclusion criteria

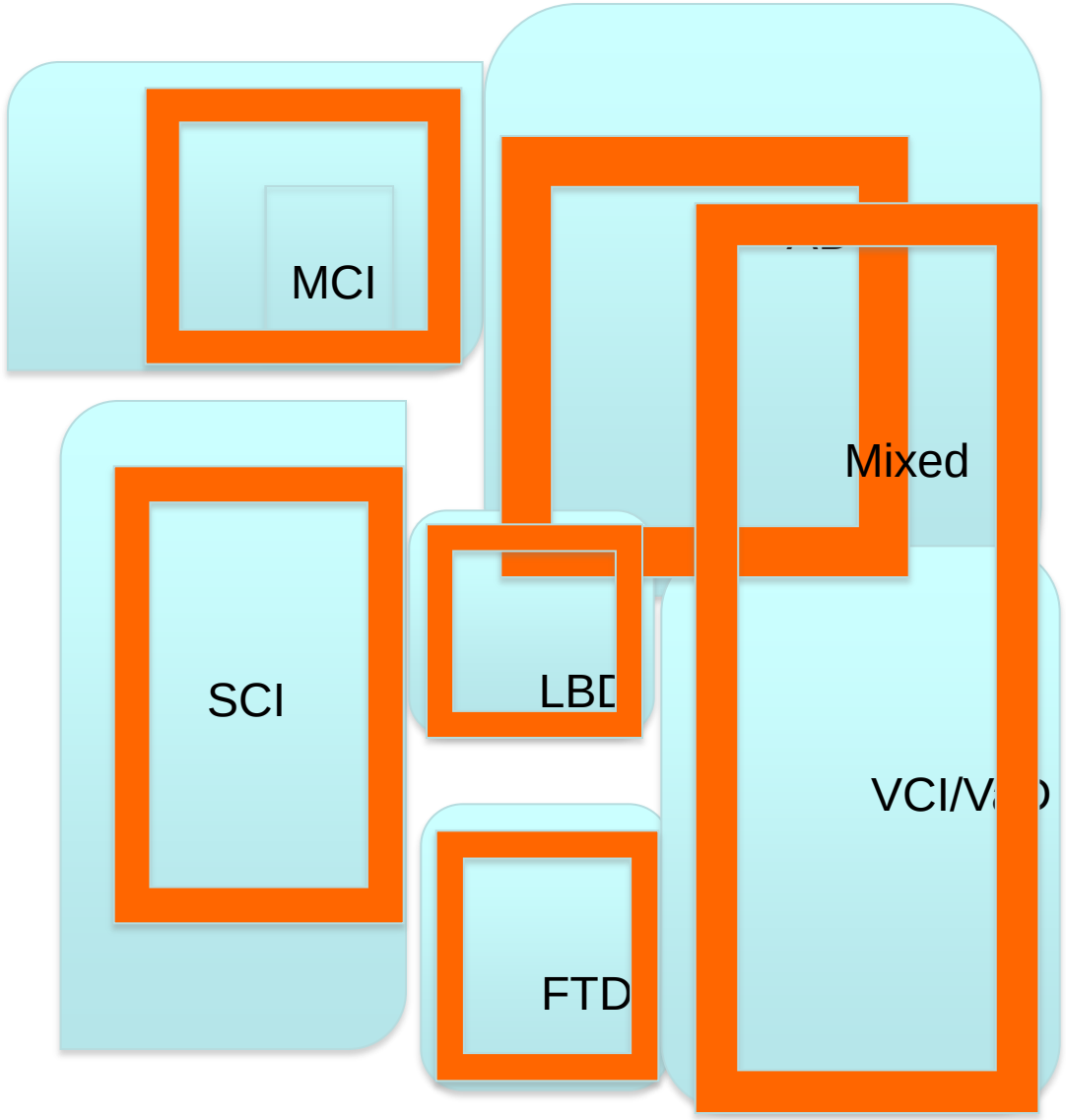
Comprimise:

- “rather broad” criteria will produce less homogeneous groups that represent most of the dementia population.

•Will include co-morbidities and mixed dementias

•Will include most mixed disease but not all.

•Will exclude other brain disease, major psychiatric, drug addiction



Subject Flow in Platform #1 - Clinical Cohorts

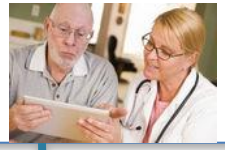
1. Recruitment Into CCNA

Note: Can be recruited into OBI, CIMA-Q as well

2. Informed Consent Signed

Shared consent procedures

3. History, Physical, Cognitive Evaluation



- iPAD/tablet clinical data (upload)
- Web-based computerized intake
- Assess inclusion/exclusion criteria
- Demographics, medical/surgical history
- Physical/Neurological examination

4. Questionnaires

- mental health
- Social
- psychiatric

5. Psychometric Testing

- National battery

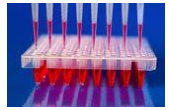
6.Biosamples

6a.Blood

6b.Saliva

6c.CSF

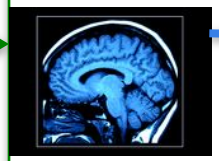
7. Sample Processing



8. Sample Shipping to Biobank

9. MRI Imaging Acquisition

10. MRI IT and Databasing



C-Brain

LORIS

11. Brain Donation Program and Follow-up in Clinic

Deep Phenotyping of the cohorts

Extensive cognitive testing

MRI scans will be collected on this cohort at 3 Tesla (2/3) and 1.5 tesla (1/3), using “Canadian Dementia Imaging Platform” sequences.

Automatic volumetry will be provided by True Positive Medical Diagnostics

Extensive biosamples- blood, saliva, urine, csf, microbiome from fecal and oral samples

Genetics: **NeuroX chip SNP screen= a genetics platform**

Planned: Longitudinal follow-up

↗brain donation program– national coordination

↗National brain exam protocol, brain banking consortium

frontiers in NEUROINFORMATICS
TECHNOLOGY REPORT
published: 20 January 2012
doi: 10.3389/fninf.2011.00037

LORIS: a web-based data management system for multi-center studies

Samir Das[1], Alex P. Zijdenbos[2], Jonathan Harlap[3], Dario Vins[4] and Alan C. Evans[1]*

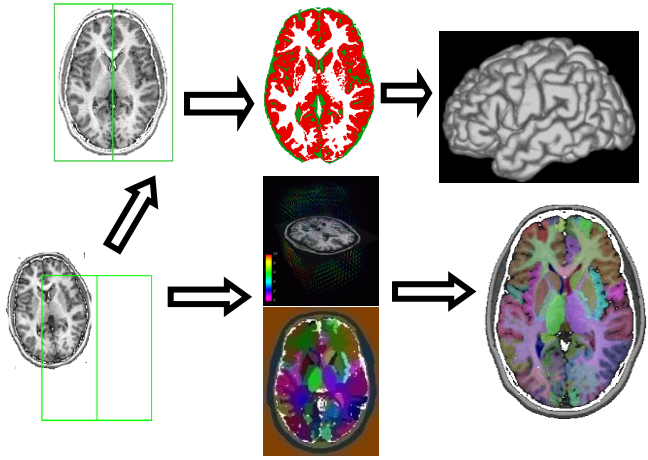
80 man-years of development
Web-based, secure data transfer of multi-site data
Generalized open-source MYSQL architecture - flexible, extensible
Applications in development, neurodegeneration (US, Europe, Asia)

Acquisition management

Project management tools
Double data entry/ range checking
Automated 3D image QC
Java-based remote 3D image QC
150 behavioral instruments
MANTIS bug-tracking

Analysis pipelines

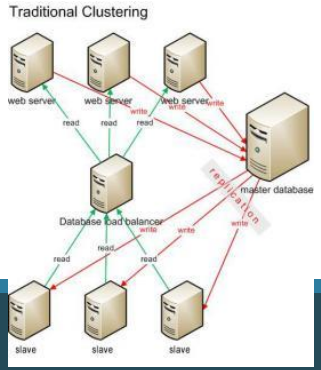
External pipelines for analysis (MNI, SPM, FSL , LONI, AFNI)
Integrated with grid-computing networks (CBRAIN, NeuGrid)



LORIS

Repository /download

Data types: behavior, clinical, imaging, genetic
On-line remote MRI browser
Data querying GUI (volumes, surfaces, behavior)
e.g. NIH database of normal brain development



Important National/ International Linkages and Opportunities

- Links with Canada's CLSA: Canadian Longitudinal Study of Aging = 30,000 in population aging study
-- as normative control group

- GAP (Global Alzheimer Platform) and the European EPAD (European Prevention of AD Consortium): CCNA as a potential Canadian partner to establish a registry and readiness cohort for clinical trials internationally

- Big Data – link with UK Dementia Platform (UKDP)
  - OECD Big Data initiative
  - Memorandum of Understanding with UKDP
-Grant application to fund these collaborations

Progress-current and future

- Tremendous “buy-in” from Canadian research scientists
- CCNA is already “on the map” nationally and internationally
- CCNA funding from CIHR planned for 5 years (April 2014-March 2019)
- Minister of Finance Budget speech (Feb. 2014) committed long term support for CCNA from Treasury Board of Canada
- This appears to allow renewal of CCNA 2019-2024 or even 2029 as necessary and after peer review.
- Goal: delivering breakthroughs in diagnosis, treatment, and improvement in quality of life of individuals with neurodegenerative diseases in Canada.