Positive Brain Health Now

A CIHR funded team initiative to investigate neurocognitive dysfunction in HIV positive individuals

CIHR awards $2,492,705 to study how to improve brain health in HIV-infected individuals.

People living with HIV worry about their memory, and with good reason. As life expectancy increases, it is becoming clear that this chronic illness commonly affects both cognition and mental health, with prevalence of impairment in these domains of 30-50% even with excellent systemic viral control. Although little is known about the burden of these symptoms in the Canadian context, the available evidence argues that these symptoms have a substantial impact on occupational function, medication adherence, quality of life, and even life expectancy. The causes of compromised brain health are likely to be a multi-factorial combination of HIV-related biological factors, co-morbidities such as aging and cerebrovascular disease, and the erosion of coping skills, physical health, and social supports resulting from the strains of living with a chronic illness. The heterogeneous, multifactorial nature of compromised brain health in HIV is both a challenge and an opportunity. A better understanding of the relationship between cognitive complaints, depression, and objectively measured cognitive impairment, and of the key factors, whether biological or personal, which relate to these presentations and to their evolution over time, will allow tailored approaches to screening and management. Characterization of this heterogeneity will also permit more focused pathophysiological studies, which will in turn inform the development of new treatments.

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Upcoming Events

Jan 31st Inaugural HIV Brain Health Monthly Video-Rounds

Developing a Clinical Platform to Study Brain Health in HIV: Overview: Lesley Fellows, Marie-Josée Brouillette, Nancy Mayo

16:00-17:00 EST; De Grandpré Communications Centre, Montreal Neurological Institute

14:00-15:00 MST; Alberta

13:00-14:00 PST; St. Paul's Hospital; BC-CfE Conference Room

8:00-9:00 AST (**FEB 1st**); Sydney Australia

Feb 28th Contracts and regulatory packages sent to all sites

Feb 28th Current approaches to diagnosis and classification of HIV-associated neurocognitive disorder: A critical summary Lucette Cysique

Mar 28th Causes of HIV-associated neurocognitive disorder: What we know and don't know Bruce Brew

Positive Brain Health Project Objectives

Our goal is to identify, understand and optimize brain health in people living with HIV focusing on cognitive impairment, its measurement, contributors and consequences. The specific objectives are:

(i) To estimate the extent to which HIV-related clinical factors and patient-centered outcomes relevant to brain health and its consequences inter-relate and evolve over time;

(ii) To contribute evidence for the validity of a brief brain health assessment approach combining both patient-reported and measured cognitive deficits;

(iii) To contribute evidence for the feasibility, effectiveness potential, and acceptability of promising interventions for optimizing brain health; and

(iv) To explore the mechanisms underpinning longitudinal change in brain health.

Participating Sites:

Montreal: Montreal Chest Institute, Clinique Médicale L'Actuel
Vancouver: St. Paul's Hospital

Recruitment:

Main platform 900 (within 2 years) + 260 Neuropsychological tests

Visits:

Baseline, 9, 18, 27 months

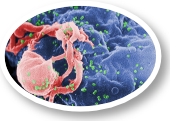
From left to right: Lesley Fellows (Neurology), Nancy Mayo (Clinical Epidemiology), Marie-Josée Brouillette (Psychiatry), Lisa Koski (Neuropsychology)

A message from the Positive Brain Health Core Team

We would like to take this opportunity to thank all of you for collaborating with us and making this initiative possible. We are thrilled to be part of this multi-disciplinary team with expertise in intersecting spheres within biomedical, clinical and population health. Since our team is literally from across the world we would like to use this forum to introduce each of our co-investigators, community and corporate partners in the newsletters to come.

We look forward to working with all of you!

An Introduction to Neurocognitive Deficits in HIV



People living with HIV worry about their memory, and with good reason. As their life expectancy increases, it is becoming clear that this chronic illness affects both cognition and mental health, even with excellent systemic viral control. Although we are only beginning to understand these emerging co- morbidities, they are likely the result of multiple interacting processes.

HIV has direct effects on the brain: highly active anti-retroviral therapy (HAART) may not fully penetrate the CNS, providing a reservoir for viral replication, and inflammation may affect brain function. Anti-retrovirals may themselves be neurotoxic, as may common co-morbidities such as aging, depression, cerebrovascular disease, substance abuse and hepatitis C infection. The experience of living with chronic infection can threaten brain health by affecting stress levels, coping, physical health, and social supports.

Although the burden of poor brain health in HIV in Canada is unknown, it is likely to be high. Recent studies in other developed countries, using comprehensive neuropsychological assessment, report a prevalence of (primarily mild) cognitive impairment of 30-50%. Even higher rates have been documented in those over the age of 50, a rapidly expanding group at the frontier of existing knowledge about the combined effects of aging and longstanding HIV infection. Depression is also common in HIV infection, with population-based prevalence of major depressive disorder estimated as high as 36%. Mood disorders can affect cognition even in otherwise healthy individuals. In HIV specifically, cognitive complaints have been associated with depressive symptoms more consistently than with objective cognitive performance. It may be that depressive symptoms and cognitive difficulties are two facets of brain dysfunction, or that depression affects cognitive performance (in life and in testing situations) through effects on attention or motivation. Impaired cognition and depression, whether together or separately, strike patients in their productive years, and can affect medication adherence, occupational and social function, quality of life, and even accelerate mortality. Progress in understanding the heterogeneous, multi-factorial nature of compromised brain health in HIV will require careful clinical characterization, including of its evolution over time, accompanied by hypothesis-driven research focused on specific clinical phenotypes. Progress in predicting, treating and mitigating the impact of poor brain health will require better, practical clinical tools and evidence-based interventions specifically tailored for people living with HIV.

The nomenclature describing cognitive impairment, and the modalities used to measure cognition vary across clinical disciplines, hindering interdisciplinary research. For this proposal, we have chosen to use the term cognitive deficit and its positive opposite, cognitive ability; we also distinguish between directly measured cognitive deficits (i.e. neuropsychological tests) and perceived cognitive deficits reported as symptoms (here measured using validated questionnaires). This method is broadly consistent with the requirements of the current diagnostic criteria for HIV-Associated Neurocognitive Disorders (HAND) . Our view of cognition departs from current diagnostic approaches by focusing on cognitive ability as a “quantity”. We propose that declines in cognitive ability compared to the individual’s own baseline will be the most useful trigger for intervention, and that stability or improvements are likely to be more important to the patient than whether they meet arbitrary diagnostic thresholds.

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Rigid use of diagnostic categories may prevent recognition of real difficulties, and limit access to useful interventions for patients with high (but deteriorating) cognitive abilities. Current approaches to diagnosis rely on neuropsychological testing. This is resource-intensive and not universally available in the Canadian context.

Front-line health care providers who must judge whom and when to refer are poorly equipped to respond to patients' concerns about cognition: What symptoms signal difficulties that warrant further investigation or intervention? What interventions are appropriate? Are there patients who do not report symptoms who nonetheless have deficits and would benefit from assessment and treatment? How should they be identified? We recognize that a key challenge in this area is to understand the link between what patients are saying, which is what matters to them, and what the objective tests indicate. Developing better ways to measure both symptoms and signs that are feasible in everyday practice, and tuned to the full range of abilities in the population is a crucial first step. While better measurement and thorough description of the clinical phenomenology and its evolution are necessary, they are not sufficient. We need to link this level of study to work on the underlying pathogenic mechanisms if we are to develop rational approaches to treatment.

People with HIV cannot afford to wait for researchers to fully understand this complexity. They are facing brain health challenges today, with real meaning for their everyday function. Research in other chronic neurological disorders has provided the tools to help these people now. In particular, research on the effects of exercise, self-management and cognitive training in healthy aging and mild cognitive impairment (MCI) shows promise in improving cognitive functions that are also commonly affected in HIV. There is more than a conceptual parallel between these conditions. Subtle pathological aging changes are found in the brains of people with HIV. We hypothesize that interventions proved useful in aging and MCI will make a difference in mood, cognitive performance, and real world outcomes such as occupational functioning and quality of life in HIV, as well as providing a "best practices" yardstick against which to judge the effects of HIV-specific interventions.

Lesley Fellows, MD, DPhil

Dr. Lesley Fellows is a neurologist specializing in disorders of cognition. She has a particular interest in the functions of the frontal lobes. Her research programme focuses on the brain basis of decision making in humans, using the tools of cognitive neuroscience. She studies how focal brain damage or neurochemical dysfunction affects all aspects of decision making, how options are generated and organized, how they are valued and compared, and how choices are made. She is also interested in more general questions about the roles of the frontal lobes in the regulation of emotion, the expression of personality traits, and the representation of past and future information. This work has relevance for understanding impaired executive function following frontal lobe injury from aneurysm rupture, stroke, or tumour growth, as well as in degenerative conditions such as Parkinson's Disease and some forms of dementia. It also provides insights into how the component processes that underly decision making are carried out in the intact brain.

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We have assembled a new team with intersecting expertise in basic and clinical HIV medicine, basic and clinical neurosciences, and health outcomes measurement and applied statistics. The proposed work will be carried out in university-based and community clinics in Montreal and Vancouver, in French and English, using epidemiologically rigorous sampling methods to ensure a broadly generalizable picture of brain health in HIV in the Canadian context. Patient-centered measures, the integral involvement of HIV community members, health care providers, and trainees, and our focus on practical interventions will ensure translational impact of the knowledge gained. The project makes extensive use of Web-based research and health care delivery tools, aiming to provide cost-effective, "clinic ready" tools to improve brain health in HIV. This project has two overarching aims, reflecting our dual goals of understanding and improving brain health in HIV, focusing on cognitive impairment, its contributors and consequences. The objectives are to contribute evidence for the validity of a brief brain health assessment approach, to estimate the extent to which HIV-related cognition-relevant clinical factors and patient-centered outcomes inter-relate and evolve over time, allowing identification of the mechanisms underpinning longitudinal change in brain health and, to contribute evidence for the feasibility, effectiveness potential, acceptability, and underlying mechanisms of promising interventions for optimizing brain health.

We will develop a multiple randomized control trial platform, an approach suitable for providing pragmatic evidence to inform clinical management of complex health conditions. A total of 900 participants recruited from 3 sites will be characterized prospectively over a 27-month period to answer questions about the evolution of outcomes of interest. All participants will be offered basic brain health information. Sub-groups of the sample will participate in pilot studies of specific, more intensive interventions to provide pragmatic evidence for feasibility, effectiveness, and comparative effectiveness. We will develop and pilot a Web-based comprehensive brain health self-management program, a physical activity intervention, and a computerized cognitive training program. All interventions will be specifically adapted to the needs of this population through an iterative process involving research participants, community members, and those involved in the front line care of people with HIV. The platform will serve as a foundation for future full-scale trials of promising interventions, and will provide a unique resource to facilitate specific, mechanism-focused sub-studies, some of which are showcased in this proposal. This work will provide needed estimates of the burden, heterogeneity, evolution, and mechanisms underlying compromised brain health in HIV, and engage a dynamic new team to understand and address this complex and important health condition.

Marie-Josée Brouillette, MD

Dr. Marie-Josée Brouillette is a psychiatrist and an Assistant Professor of Medicine at McGill University. Her primary area of interest is the effect of HIV infection on the brain. She has been a member of the Immunodeficiency Service of the Royal Victoria Hospital since 1990. She has led three successful clinical studies in the field of HIV & cognition. The first study, a prospective observational study investigated cognitive change over one year in HIV+ individuals at risk (over the age of 40 with a nadir CD4 cell count below 200). The second study aimed to describe the clinical characteristics of HIV+ individuals with cognitive difficulties and to assess changes in neurocognitive functioning over 6 months following modifications in HIV treatment resulting from the investigation. The third study aims to develop a brief clinical tool to measure cognitive ability.

Community Partners

Ken Monteith is the Executive Director of COCQ-SIDA (la Coalition des organismes communautaires québécois de lutte contre le sida). COCQ-SIDA's mission is to encourage, support, consolidate and promote autonomous community action against HIV/AIDS in Québec. Thirty-eight groups from across Québec are members of COCQ-SIDA.

Trained as a lawyer, Ken worked in the community youth sector as Legal Coordinator and Executive Director of Head & Hands / À deux mains for nine years before joining AIDS Community Care Montreal (ACCM) in 1999 as Executive Director. Ken left ACCM in 2008 to take up his current position at COCQ-SIDA. He is COCQ-SIDA's representative to the Canadian Treatment Action Council (CTAC) and was appointed to the federal Ministerial Council on HIV/AIDS in 2003.

He holds degrees in Industrial Relations, Common and Civil Law from McGill University and was a member of the Québec Bar from 1991 to 2001, when he resigned to devote himself more fully to his community work on HIV/AIDS.

Ken Monteith was diagnosed with advanced HIV infection in 1997.

Ken Monteith,
Directeur general, COCQ-SIDA
www.cocqsida.com

Contact Information

Marie-Josée Brouillette, Co-Principal Investigator

Marie-josee.brouillette@mcgill.ca

Lesley Fellows, Co-Principal Investigator

Lesley.fellows@mcgill.ca

For any questions on regulatory, contracts, study procedure or communications please contact:

Sahar Saeed, MSc CCRP

sahar@cr-solutions.ca

514-945-0224