HIV-Related Cognitive Impairment

What is HIV-related cognitive impairment?

The Human Immunodeficiency Virus (HIV) can infect the brain and impair central nervous system (CNS) function. With the advent of antiretroviral therapies, the most severe forms of HIV-associated dementia significantly decreased in prevalence. The subtler forms of HIV-associated neurocognitive disorders, however, remain frequent.

The major focus of our research is the impact of HIV on the central nervous system and cognitive functioning. Cognitive impairment in HIV is categorized into three groups?

- Asymptomatic Neurocognitive Impairment (ANI),
- Mild Neurocognitive Disorder (MND), and
- HIV-associated Dementia (HAD).

Patients with ANI demonstrate cognitive impairment on formal neuropsychological tests but experience no observable impairment of everyday functioning. More severe than ANI, patients with MND demonstrate mild-to-moderate impairment on formal testing and mild-to-moderate impairment in activities of daily living. The most severe form of cognitive impairment – HAD – includes moderate-to-severe cognitive impairments as well as difficulty with daily living activities.

Ever since antiretroviral therapy became widely available in developed countries, HAD has become quite rare, observed in only 2 to 3 percent of patients in research studies. Additionally, though patients are observed to experience fluctuation in cognitive impairment, progressive decline is rare, although HIV-associated cognitive deficits become more likely with increasing age. Cognitive impairment is also linked to disease severity, measured through CD4 counts and onset of AIDS.

Our work is centered on the hypothesis that HIV virus enters the CNS early on, causing inflammation and establishing a viral reservoir in the CNS that resists eradication with antiretroviral drugs. In our local Aging with HIV cohort, we are exploring the link between aging, HIV, and the risk for neurodegenerative disorders, principally, Alzheimer’s disease. We are also evaluating the link to comorbidities, such as insulin resistance, to cognitive decline in HIV. Our aging cohort is composed of nearly 100 subjects over 60 years of age living with HIV as a chronic condition. Here, we are investigating risk for cognitive impairment longitudinally with neuropsychological assessments, neurological examinations and MRI imaging. There is little data currently available on the impact of the disease on patients in this age range, who have been living with chronic HIV
sometimes for decades. With our work at UCSF, we hope to elucidate the long-term CNS impact of HIV on our older HIV-positive population.

Through our national and international collaborations, we are also investigating the early impact of HIV and antiretroviral therapy (ART) on the CNS. Dr. Valcour has established enduring collaborations with the SEARCH-Thailand team, the U.S. Army's Armed Forces Research Institute of Medical Sciences (AFRIMS), as well as the Thai Red Cross (TRCARC). Together with these partners, Dr. Valcour has launched investigations into the CNS impact of acute HIV infection (within weeks of infection), the role of HIV DNA in peripheral monocyte populations, and the developmental consequences of HIV infection on cognition in children and the benefits of early ART intervention.

UCSF HIV (neuroAIDS) Studies

The UCSF HIV Over 60 Cohort: This study aims to understand brain health in people living with HIV over the age of 60. Specific questions being addressed relate to the frequency of cognitive impairment, brain atrophy and functional consequences of aging with HIV. Particular emphasis is placed on risk for neurodegenerative disorders, such as Alzheimer's disease.

The UCSF HIV Elders Study: The UCSF HIV Elders Study is a new behavioral intervention study examining the efficacy of a mindfulness based stress reduction (MBSR) course in the management of symptoms associated with attention, executive functioning, stress and anxiety among HIV+ individuals aged 60 years and above. This study is located in the San Francisco Bay Area and includes neurological examinations, neuropsychological testing, geriatric syndrome assessment, functional testing, multimodal brain imaging and an 8-week MBSR course led by a certified MBSR instructor at the UCSF Osher Center for Integrative Medicine. Read more...[8]

Collaborative Projects underway Internationally

Africa:

* African Cohort Study (AFRICOS): The AFRICOS study will investigate cognition in people living with HIV in Tanzania, Uganda, Kenya and Nigeria. It is being launched in the fall of 2012. Read more...[9]

Thailand and Cambodia:

(for more details, please go to www.SEARCHThailand.org [10])

* SEARCH 001: Predictors of Neurocognitive Decline and Survival in HIV-infected Subjects. This completed study evaluated immunological, virological and proteomic profiles of 30 HIV patients initiating HAART for the first time. Half of the subjects had dementia. Clinical data remain available for analyses.
• SEARCH 002: Establishing normal values for neuropsychological testing in HIV-negative Thais. This study is establishing normative data for neuropsychological tests used to evaluate HIV brain injury in Bangkok. Over 500 subjects have been enrolled.

• SEARCH 003: A 72-week randomized clinical trial comparing the safety and efficacy of three initial antiretroviral regimens—GPO-VIR S (d4T/3TC/NVP) for 24 weeks followed by GPO-VIR Z (AZT/3TC/NVP) vs GPO-VIR Z vs TDF/FTC/NVP. Work from this study measures mitochondrial risks of short-duration d4t as an initial treatment for HIV (6 months). Primary outcomes include neuropathy, anemia, and lipodystrophy. Enrollment is complete.

• SEARCH 005: Prevalence and risk factors of HIV-associated neurocognitive impairment and psychiatric comorbidities in HIV-1 infected Thai individuals with undetectable viral load in the HAART era. This completed study estimated the frequency of cognitive impairment in patients well-controlled on NNRTI-based treatment in the 2NN cohort.

• SEARCH 007: HIV-1 Specific Immune Responses in Thai Individuals with HIV Dementia. The goal of this work is to determine the role of HIV-specific T-cell responses in HIV-associated dementia.

• SEARCH 010: Establish and characterize an acute HIV infection cohort in a Thai high risk population. This study will identify patients who have been infected for less than 4 weeks and complete intensive evaluations, including immunological markers, virological markers, gut biopsy, lumbar puncture, MRI/MRS, neuropsychological and psychiatric evaluations, assessment of willingness to participate in vaccine trials, and tracking of contacts.

• SEARCH 011: Peripheral Reservoir of HIV DNA in Monocytes Pivotal to Cognition in HIV. Here we are determining the impact of monocyte HIV DNA on (1) neuropsychological testing, (2) CSF markers of immune activations, (3) CSF HIV RNA levels, (4) inflammation by MRS.

• SEARCH 012: Neurodevelopment and imaging among HIV-infected Children from the PREDICT study. This project aims to determine the neurodevelopmental impact of deferring the initiation of HAART in children until immunological suppression occurs.

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Research Partners in Bangkok, Thailand

• Southeast Asia Research Collaboration with Hawaii (SEARCH) [10]
• Thai Red Cross AIDS Research Centre (TRCARC) [17]
• Armed Forces Research Institute of Medical Sciences (AFRIMS) [18]