

# Resting Cerebral Blood Flow as a Biomarker of HIV in the Brain

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## Background

Neuroimaging, in particular global resting cerebral blood flow (rCBF), could be a preclinical biomarker of the effects of HIV in the brain. Previous studies have demonstrated hypoperfusion within cortical and subcortical structures in HIV-infected (HIV+) on highly active antiretroviral therapy (HAART) compared to HIV-uninfected (HIV-) subjects (1, 2). These HIV associated decreases in rCBF have been seen prior to changes in neurologic examination, neuropsychological performance testing, or structural imaging. In a cross sectional analysis we studied the association of HAART treatment on rCBF in HIV+ participants (both naïve and on a stable HAART regimen). Within a smaller subset we longitudinally assessed individuals prior to and 3-5 months after starting HAART. We hypothesized that HAART would lead to a greater normalization in rCBF in HIV+ participants.

## Methods

rCBF measurements were obtained from 26 seronegative controls (SNC) and 39 HIV+ subjects at 3 Tesla (Siemens) scanner using an arterial spin labeling (ASL) technique (3). HIV+ subjects were further subdivided into either naïve (n=19) or on stable HAART regimen for > 3 months (mean = 27 months) (n= 20). A subset of the HIV+ naïve participants (n=9) were studied 3-5 months after starting medications. Analysis of variance (ANOVA) for resting CBF changes was performed and subsequent paired *t*-tests utilized with *p* values significant if *p* < 0.05.

## Results

No significant differences in age, sex, or education were observed between HIV- and HIV+ subjects. HIV+ naïve participants had a higher viral load (*p*=0.0001) and CD4 nadir (*p*=0.001) than HIV+ subjects on HAART. Overall, HIV- controls had a significantly higher mean rCBF ( $61.7 \pm 1.7$  ml/100gm/min) compared to HIV+ participants ( $48.4 \pm 1.9$  ml/100gm/min).

Global rCBF was significantly diminished in HIV+ naïve patients ( $44.8 \pm 1.9$  ml/100gm/min) compared to HIV+ subjects on stable HAART ( $52.6 \pm 2.0$  ml/100gm/min) (Figure 1A). CBF was diminished throughout the brain with no region significantly higher for HIV+ subjects compared to HIV- controls (Figure 1C). Longitudinally, each HIV+ naïve subject had a decrease in viral load and an increase in rCBF after starting HAART (Figure 1B). A strong inverse correlation (will need to compute R) existed between these variables.

## Conclusions

HIV infection is associated with diminished global resting cerebral blood flow (rCBF). Initiation of HAART led to an increase in global rCBF as well as improved virological control. The mechanism of etiology for these observed decreases in brain perfusion requires further detailed evaluation. Resting cerebral perfusion may provide a sensitive biomarker for effects of HAART in the brain.

## References

1. Ances BM et al. (2009) *Neurology*, 73(9):702-8.
2. Ances BM et al. (2006) *Neurology*, 66(6):862-6.
3. Wang JJ et al. (2005) *Radiology*, 235(1):218-28

