Poster # 463

Vascular Endothelium and Neurological Performance during Primary HIV Infection

Urday S[1], Robertson K[2], Li FY[1], Chow FC[3], Peterson J[3], Nitta EM[4], Price RW[3], Hsue PY[4], Spudich S[1]

[1]Department of Neurology, Yale University School of Medicine, New Haven, CT; [2]Department of Neurology, University of North Carolina, Chapel Hill, North Carolina; [3]Department of Neurology, School of Medicine, University of California, San Francisco, CA; [4]San Francisco General Hospital Cardiology Division, University of California, San Francisco, CA

Background

• HIV-infected individuals on optimal anti-retroviral therapy (ART) have increased rates of premature vascular diseases and neurocognitive decline

• We hypothesize that:

(i) Cerebrovascular injury resulting from persistent HIV-induced inflammation is one mechanism for neurocognitive decline

(ii) Asymmetric dimethylarginine (ADMA), a plasma biomarker of endothelial dysfunction and promising predictor of cerebrovascular disease and dementia[1], may play a role in the pathophysiology of neurocognitive impairment in HIV

Methodology

• 15 subjects with primary HIV infection (PHI, < 1 yr since HIV transmission) underwent both cardiovascular (CV) and neurologic testing

• Neurological performance measures: total z-score (based on normed performance on 11 tests) and brief NPZ-4 (based on a subset of 4 tests)

• Vascular measures: (1) carotid artery intima-media thickness (IMT); (2) brachial artery flow-mediated dilation (FMD); (3) hyperemic velocity; and (4) ADMA (Oxonon BioAnalysis, CA)

• Examined correlations between CV and neurologic measures weighted by the number of repeated visits per each subject with the use of the Pearson correlation coefficient

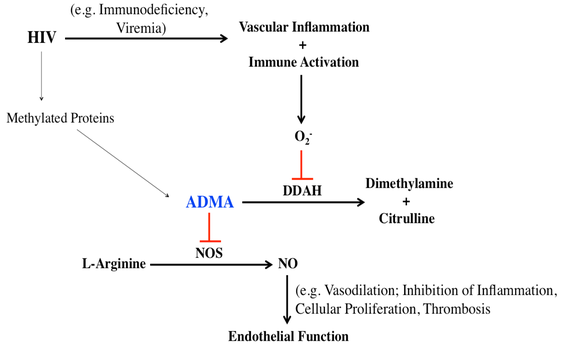


Figure 1. Mechanism of ADMA accumulation in HIV infection[2]

Results

Table 1. Subject Characteristics at Baseline

	Total N = 15 N (%) or Median (IQR)
Age, y	37 (32, 47)
CD4 count, cells/μL	474 (361, 656)
Plasma HIV RNA, $\log_{10}$ copies/mL	4.59 (3.64, 4.94)
CSF HIV RNA, $\log_{10}$ copies/mL	2.58 (1.69, 3.33)
Enrolled at days post-infection	93 (77, 153)
ART naive	15 (100)
Interval between CV and Neuro testing, d	31 (16, 75)
Duration of follow-up, d	364 (0, 641)
Systolic Blood Pressure, mm Hg	125 (104, 132.75)
Diastolic Blood Pressure, mm Hg	74 (65, 82.25)

Figure 2. Distribution of ADMA and IMT in cohort

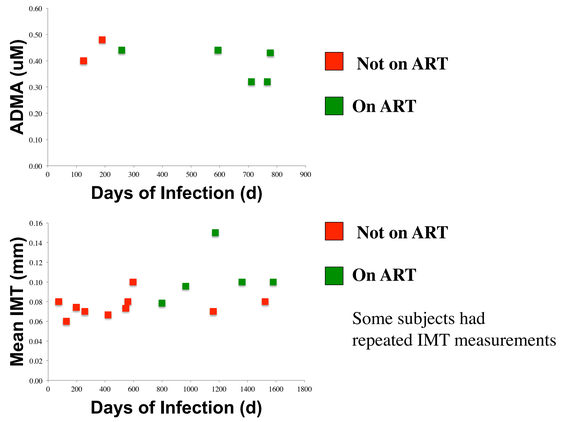


Figure 3. Higher ADMA correlated with worse neuropsychological performance, assessed by NPZ-4.

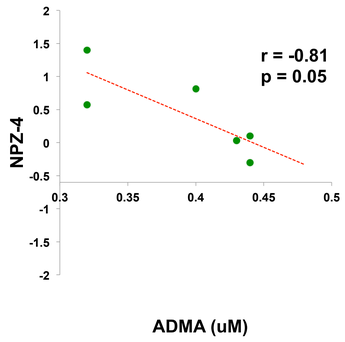
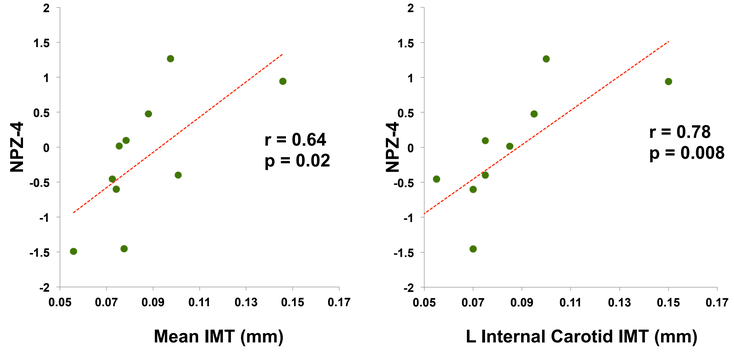


Figure 4. Unexpectedly, greater IMT correlated with better NPZ-4. No associations were found between FMD or hyperemic velocity and neurologic measures



Conclusions

• In an exploratory analysis, higher ADMA levels, suggestive of more severe endothelial dysfunction, inversely correlated with neuropsychological performance

• A seemingly paradoxical association between increased IMT, another surrogate marker of atherosclerosis, and better neuropsychological performance warrants further study

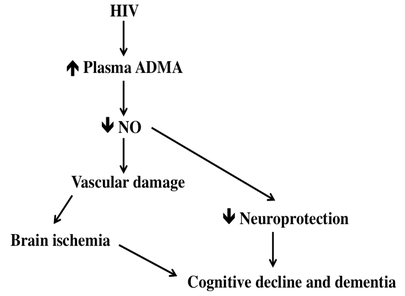


Figure 4. Possible link between ADMA and neurocognitive decline in HIV (Modified with permission from Asif et al.[1])

Future Directions

• Examine the impact of starting ART during primary HIV infection on ADMA and neuropsychological performance

• Examine the relationship between CV and neurologic measures in chronically-infected patients and elite suppressors

[1] Asif et al. Asymmetric Dimethylarginine: A possible link between Vascular Disease and Dementia. Current Alzheimer Research. 2013

[2] Parikh et al. Elevated Levels of Asymmetric Dimethylarginine are Associated with Lower CD4+ Count and Higher Viral Load in HIV-infected Individuals. Atherosclerosis. 2013; 229 (1)

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