439

Greater CSF HIV Reduction and CSF Rapid Decay Associated with Improved Neurocognition

Kevin R. Robertson[1], Natalie M. Bowman[2], Sarah B. Joseph[1], Prema Menezes[1], Nisha Bhatia[4], Christopher Lippincott[1], Michael Vinikoor[1], Joseph Eron[1], Serena Spudich[3], Ronald Swanstrom[1], Richard W. Price[3]
1. University of North Carolina at Chapel Hill, North Carolina, US, 2.Yale University, New Haven, Connecticut, US 3. University of California San Francisco, San Francisco, California, US

Kevin Robertson, Ph.D.
Neurology, School of Medicine
Chapel Hill, NC 27599-7025
kevinr@neurology.unc.edu
Ph 919 966 5522
Fax 919 966 2922

This research was supported by the University of North Carolina at Chapel Hill Center for AIDS Research (CFAR), an NIH funded program P30 AI50410, and the THINC project P01MH094177 from National Institute of Mental Health

ABSTRACT

Background.
HIV Associated Neurocognitive impairment remains problematic despite suppressive antiretroviral therapy (ART). Underlying low level HIV infection likely persists in the central nervous system (CNS) and may sustain inflammation causing neuronal damage. We sought to better understand the dynamics of HIV in the cerebrospinal fluid (CSF) during treatment initiation and the relationship to neurocognitive outcomes.

Methods.
In THINC (the HIV Tropism, Persistence, Inflammation and Neurocognition in Therapy Initiation cohort) treatment-naïve patients initiating ART with CD4 < 400 were administered neurocognitive testing (NP) and lumbar puncture (LP) at baseline. A follow-up LP was performed after 2-4 weeks on ART, and a neurocognitive follow-up was performed after 24 weeks on ART. The neurocognitive battery assessed Premorbid/language, Fluency, Executive, Learning, Memory, Speed of Processing, and Fine motor domains. We correlated change in total z score with overall change in log CSF HIV RNA, and decay as measured by change in CSF HIV RNA divided by days on ART to estimate the association of neurocognitive performance with CSF viral load and CSF decay.

Results.
Of 38 patients who underwent baseline NP and LP, 30 also received the follow-up LP and 27 also received the follow-up NP. The total z score across the neurocognitive battery at baseline had a mean of -0.91 (range -2.7 to 0.49; SD 0.66), and the mean change (computed from follow up minus baseline so that positive scores reflect improvement) was .06 (range -0.71 to 1.16; SD 0.39). The baseline log CSF HIV RNA median was 3.14 (n=38, range 1.04 to 5.58; SD 1.06), and the median change (positive numbers reflect improvement) was 3.27 (n=26, range 1.69 to 5.58; SD 1.04). There was a significant correlation between greater reduction in CSF HIV RNA and total z score change (r= .51, p<.05; see graph). CSF decay rate % was significantly associated with total z score change (r=.53, p<.05). However, no significant correlations with baseline total z score were found with baseline CSF HIV RNA, change in CSF VL, or CSF decay.

Conclusions.
A greater reduction and more rapid decay of CSF HIV after ART initiation was related to greater improvement in neurocognitive functioning after initiating ART. Reduced viral load in the CNS likely reduces ongoing inflammatory processes causing injury to neurons, resulting in relatively improved neurocognition.

INTRODUCTION

HIV Associated Neurocognitive impairment remains problematic despite suppressive antiretroviral therapy (ART). Underlying low level HIV infection likely persists in the central nervous system (CNS) and may sustain inflammation causing neuronal damage.

In THINC (the HIV Tropism, Persistence, Inflammation and Neurocognition in Therapy Initiation cohort), we sought to better understand the dynamics of HIV in the cerebrospinal fluid (CSF) during treatment initiation and the relationship to neurocognitive outcomes.

METHODS

THINC Subjects

- Antiretroviral naïve
- UNC, UCSF, Yale
- CD4+ < 400 cells/mm^3
- Lumbar Puncture (LP)
- Neurocognitive battery (NP)

- LP+NP at Baseline
- LP at 2 weeks
- NP at 24 weeks

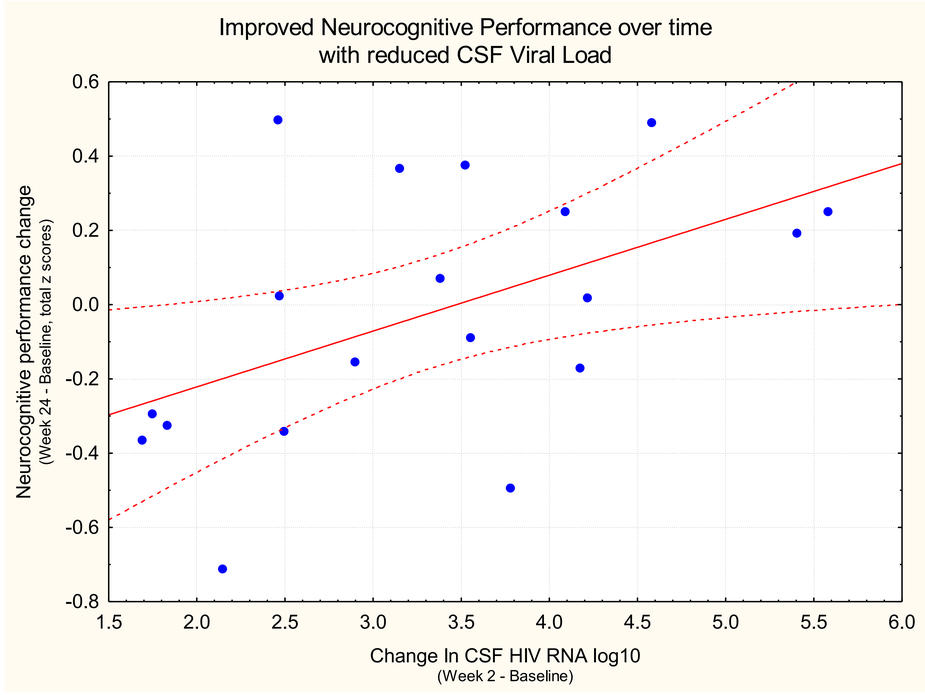
- NP Change = (time 2 – time 1, positive scores reflect improved)
- CSF Decay Rate = (Baseline CSF HIV RNA – Follow up CSF HIV RNA)/ Baseline CSF HIV RNA) / Days on Therapy

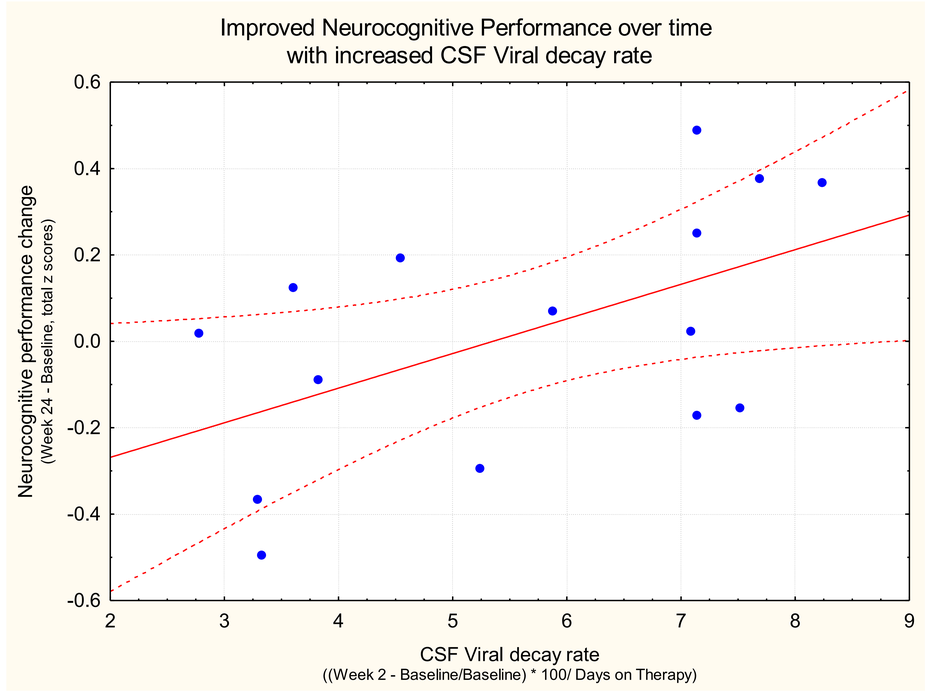
Demographics

- ART Naïve cohort
- Baseline LP+NP, n=38
- Follow LP+NP, n=30
- Gender
  - Male 26 (87%)
  - Female 4 (13%)
- Age 37 (20-63) years
- Education 13 (9-17) years

Neurocognitive Battery

Gross / Fine Motor
Timed Gait, Grooved Pegboard
Language
WRAT-4 Reading Test
Verbal Learning
HVLT-R
Verbal memory
HVLT-R delayed recall
Speed of Information Processing
Trailmaking A, Digit Symbol
Executive Functioning
Stroop, Trailmaking B, Verbal Fluency
Attention/Working Memory
Symbol Search
Functional Status
Activities of Daily Living Scale





RESULTS

ART Initiation in Naive

CSF

- CSF HIV RNA log
- baseline 3.14 (range 1.04-5.58;SD 1.06)
- change 3.27 (range 1.69-5.58;SD 1.04)
- week two 1.60 (range .95-4.14;SD 3.39)

Neurocognitive total score

- total z score
- baseline -.91 (range -2.7 to .49; SD .66)
- change .06 (range -.71 to 1.16; SD.39)
- week 24 -.71 (range -1.66-.35;SD .66)

•Reduced CSF Viral Load

- Reduced CSF HIV RNA
- Improved total z score
- (r= .51, p<.05)

•Faster CSF Decay rate

- Increased CSF HIV RNA decay rate
- Improved total z score
- (r=.53, p<.05)

CONCLUSIONS

Decreased CSF HIV viral load and Increased CSF HIV rate of decay

are associated with later Improved Neurocognitive Functioning

A greater reduction and more rapid decay of CSF HIV after ART initiation was related to greater improvement in neurocognitive functioning six months after initiating ART.

Reduced viral load in the CNS likely reduces ongoing inflammatory processes causing injury to neurons, resulting in relatively improved neurocognition.

THINC would like to acknoweldge Sarah Yosief, Laura Kincer, Elaine Yip, Jessica Margolis, Alex Russell for working on this study and our participants for making science possible.