

# LONG-TERM NEUROLOGIC EXAM FINDINGS IN PEOPLE DIAGNOSED AND TREATED DURING ACUTE HIV INFECTION

Kathryn B. Holroyd<sup>1</sup>, Tyler Hamby<sup>2,3</sup>, Carlo Sacdalan<sup>4,5</sup>, Somchai Sriplienchan<sup>4</sup>, Pathariya Promensa<sup>4</sup>, Luxe-naree Poonpitak<sup>4</sup>, Netsiri Dumrongpisutikul<sup>6</sup>, Eugene Kroon<sup>4</sup>, Sandhya Vasan<sup>2,3</sup>, Robert Paul<sup>7</sup>, Ferron O'Campo<sup>8</sup>, Lydie Trautmann<sup>2,3</sup>, Phillip Chan<sup>9</sup>, Serena Spudich<sup>9,10</sup> on behalf of the RV254/SEARCH 010 Study Team

1. Department of Neurology, Columbia University Irving Medical Center, New York, NY, USA 2. Military HIV Research Program, Walter Reed Army Institute of Research, Silver Spring, MD, USA 3. Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., Bethesda, MD, USA 4. SEARCH Research Foundation, Bangkok, Thailand 5. Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand 6. Department of Radiology, Diagnostic Division, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand 7. Faculty of Psychological Sciences, Missouri Institute of Mental Health, University of Missouri-St. Louis, St. Louis, MO, USA 8. Department of Neurology, University of Toronto, Toronto, Canada 9. Department of Neurology, Yale University School of Medicine, New Haven, CT, USA 10. Yale Center for Brain and Mind Health, Yale University School of Medicine, New Haven, CT, USA

## BACKGROUND

- Neurologic exam (NE) abnormalities are common in people living with HIV (PLWH)
- Little work has evaluated neurologic signs and symptoms in people diagnosed and treated during acute HIV infection (AHI)
- One prior study found NE abnormalities in 53% of people in the 12 weeks after AHI diagnosis, and 9% at 24 weeks

## METHODS

- We retrospectively evaluated serial NE findings for RV254 AHI cohort participants in Bangkok
- Standardized objective NE (extra-ocular movements, strength, detailed motor exam, sensation, reflexes, and coordination) were performed at week 0 (AHI), 12, 96, and 288

- **Sensory abnormality** was defined as abnormality in light touch, vibration, or proprioception in lower extremities

- Speech
- Facial expression
- Resting tremor
- Action or postural tremor on hands
- Rigidity
- Finger taps
- Hand movement
- Rapid alternative movement of hands
- Leg agility
- Arising from chair
- Posture
- Gait
- Postural instability
- Slow movement

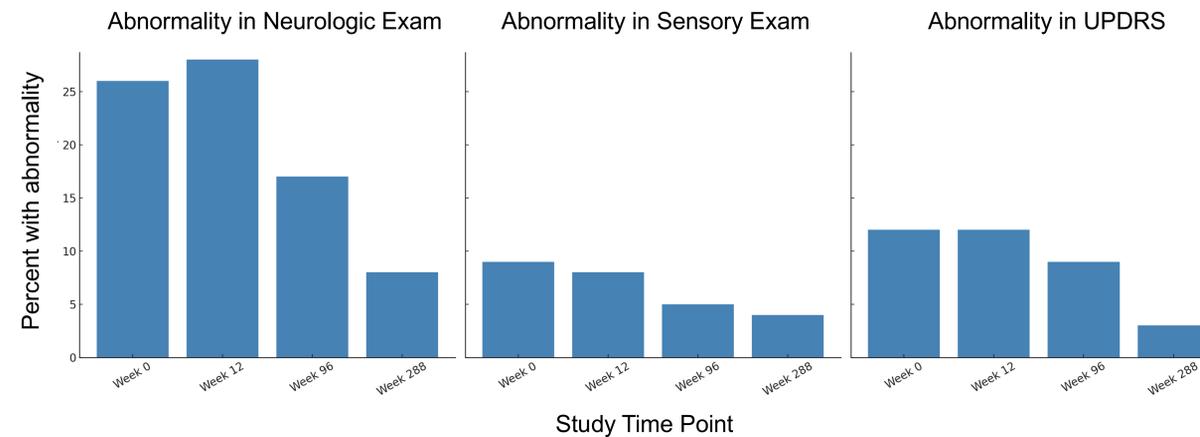
- **Detailed motor exam** was measured using the motor Unified Parkinson's Disease Rating Scale (**UPDRS**)
- HIV parameters, syphilis, Hepatitis C (HCV), and Hepatitis B (HBV) testing were also performed at each visit
- Radiologist MRI brain reports were reviewed at week 0 and 96
- Abnormal MRIs were categorized into white matter hyperintensities, atrophy out of proportion to age, gliotic change, or other intraparenchymal abnormality based on review of radiologist reports
- Chi-square tests were used to assess factors associated with abnormal NE at each visit. Longitudinal models used generalized estimating equations with logistic regression

## RESULTS

- At enrollment, 610 participants (97.6%) were male with a median age of 26.5
- 37% were in Feibig stage 1-2, and 63% in stage 3-5
- 81 participated in analytical treatment interruption trials (ATI) during follow-up

*Objective abnormalities on NE frequently manifest during AHI, particularly in domains of neuropathy and fine motor movements, though few persist at long-term follow-up. HCV co-infection, higher VL, CD4:CD8 T-cell ratio, and older age count also associate with NE abnormalities.*

### Abnormalities in neurologic exam findings across longitudinal follow-up



### Analysis of Factors Associating with Abnormal Neurologic Exam at any Visit

| Comparison                                  | Full Neurologic exam |                  | Neuropathy Exam   |                  | UPDRS              |                  |
|---|----------------------|------------------|-------------------|------------------|--------------------|------------------|
|   | OR (95% CI)          | p                | OR (95% CI)       | p                | OR (95% CI)        | p                |
| Week: 12 vs. 0                              | 1.94 (1.02, 3.68)    | <b>0.043</b>     | 1.78 (0.67, 4.71) | 0.247            | 2.54 (1.02, 6.32)  | <b>0.045</b>     |
| Week: 96 vs. 0                              | 1.09 (0.54, 2.20)    | 0.806            | 1.30 (0.45, 3.72) | 0.627            | 1.73 (0.65, 4.59)  | 0.271            |
| Week: 288 vs. 0                             | 0.32 (0.15, 0.70)    | <b>0.004</b>     | 0.86 (0.29, 2.60) | 0.796            | 0.29 (0.08, 1.00)  | <b>0.050</b>     |
| Sex at Birth: Female vs. Male               | 2.19 (1.14, 4.23)    | <b>0.019</b>     | 0.81 (0.22, 3.00) | 0.747            | 5.36 (2.32, 12.41) | <b>&lt;0.001</b> |
| Age in Years at Enrollment                  | 1.03 (1.02, 1.05)    | <b>&lt;0.001</b> | 1.05 (1.02, 1.07) | <b>&lt;0.001</b> | 1.02 (1.00, 1.04)  | 0.125            |
| Feibig stage at Enrollment: 3-5 vs. 1-2     | 1.28 (0.95, 1.71)    | 0.100            | 1.34 (0.86, 2.10) | 0.199            | 1.02 (0.70, 1.49)  | 0.905            |
| CD4 T-Cell Count at Enrollment              | 1.00 (1.00, 1.00)    | 0.258            | 1.00 (1.00, 1.00) | 0.536            | 1.00 (1.00, 1.00)  | 0.437            |
| CD8 T-Cell Count at Enrollment              | 1.00 (1.00, 1.00)    | 0.341            | 1.00 (1.00, 1.00) | 0.449            | 1.00 (1.00, 1.00)  | 0.134            |
| CD4/CD8 Ratio at Enrollment                 | 0.89 (0.60, 1.31)    | 0.549            | 1.39 (0.86, 2.25) | 0.173            | 0.47 (0.26, 0.85)  | <b>0.013</b>     |
| Viral Load at Enrollment, Log Transformed   | 1.07 (1.00, 1.13)    | <b>0.044</b>     | 1.10 (1.00, 1.20) | 0.051            | 1.10 (1.00, 1.19)  | <b>0.039</b>     |
| Hepatitis C at Enrollment: Yes vs. No       | 3.77 (2.34, 6.07)    | <b>&lt;0.001</b> | 1.09 (0.27, 4.47) | 0.905            | 3.28 (1.17, 9.17)  | <b>0.023</b>     |
| Syphilis at Enrollment: Yes vs. No          | 0.93 (0.67, 1.30)    | 0.685            | 0.94 (0.57, 1.54) | 0.800            | 1.19 (0.78, 1.81)  | 0.411            |
| Illegal Drug Use at Enrollment: Yes vs. No  | 0.92 (0.71, 1.20)    | 0.556            | 0.86 (0.54, 1.35) | 0.502            | 1.07 (0.76, 1.52)  | 0.697            |
| ART Regimen: MVC in Weeks 0-288: Yes vs. No | 1.05 (0.74, 1.48)    | 0.778            | 1.20 (0.72, 1.99) | 0.484            | 1.20 (0.78, 1.85)  | 0.410            |

## RESULTS

### Neurologic Exam

- There were 703, 493, 667, and 560 participants with NE data at weeks 0, 12, 96, and 288
- Viral load suppression at each time point ( $\leq 50$  copies/mL): 0%, 65%, 98%, 99%
- Abnormality in NE was reported in 26%, 28%, 17%, and 8% at each time point
- Most abnormalities were seen in sensory (9%, 8%, 5%, 4%) and UPDRS (12%, 12%, 9%, 3%)
- No difference in NE for participants in ATI vs without

### Associations with abnormal neurologic exam

- During **AHI**, **HCV co-infection** associated with abnormal NE ( $p=0.006$ )
- At **long-term follow-up**, **higher CD4:CD8 ratio** was associated with abnormal NE at that visit ( $p=0.035$  week 96,  $p=0.021$  week 288), driven by **lower CD8 T-cell count** ( $p=0.016$  week 96,  $p=0.067$  week 288).
- At week 288, **female sex** and **Maraviroc** use, also associated with abnormal neurologic exam ( $p<0.001$ )

### Multivariable analysis (all visits)

- **HCV infection**, **older age**, and **female sex** associated with abnormal **NE** ( $p<0.001$ ,  $p<0.001$ ,  $p=0.019$ )
- **Older age** associated with abnormal **neuropathy exam** ( $p<0.001$ )
- **Lower CD4:CD8 ratio** at enrollment, **higher viral load** at enrollment, **HCV co-infection**, and **female sex** associated with abnormal **UPDRS** ( $p=0.013$ ,  $p=0.039$ ,  $p=0.023$ ,  $p<0.001$ )

### Neuroimaging

- Of those with MRIs, 16% had abnormalities at week 0, and 24% at week 96
- Abnormal MRI at week 0 associated with abnormal **UPDRS** at any visit ( $p=0.039$ )

| MRI Result                                 | Week 0       | Week 96      |
|--|--------------|--------------|
| Normal                                     | 179 (83.64%) | 129 (75.88%) |
| Nonspecific White Matter Hyperintensities  | 24 (11.21%)  | 29 (17.06%)  |
| Diffuse Mild Atrophy                       | 6 (2.80%)    | 5 (2.94%)    |
| Ischemic Stroke                            | 2 (0.93%)    | 3 (1.76%)    |
| Other Abnormality (DVA, Mass, Empty Sella) | 3 (1.40%)    | 4 (2.35%)    |
| Missing                                    | 489 (69.56%) | 497 (74.51%) |