Neuropsychiatric Changes in People with HIV With or Without Long COVID After SARS-CoV-2 Infection

Abstract # 750

Phillip Chan[1,2], Tyler Hamby[3,4], Luxe-naree Poonpitak[5], Ferron Ocampo[5], Carlo Sacdalan[5,6], Pathariya Promsena[5,6], Eugène Kroon[5], Somchai Sriplienchan[5], Nittaya Phanuphak[7], Donn Colby[3,4], Trevor A. Crowell[3,4], Lydie Trautmann[3,4], Serena Spudich[1,2], Robert Paul[8] on behalf of the RV254/SEARCH 010 Study Team

1. Department of Neurology, Yale University School of Medicine, New Haven, CT, USA; 2. Yale Center for Brain and Mind Health, Yale University School of Medicine, New Haven, CT, USA; 3. U.S. Military HIV Research Program, CIDR, Walter Reed Army Institute of Research, Silver Spring, MD, USA; 4. Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., Bethesda, MD, USA; 5. SEARCH Research Foundation, Bangkok, Thailand; 6. Research Affairs, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand; 7. Institute of HIV Research and Innovation (IHRI), Bangkok, Thailand; 8. Faculty of Psychological Sciences, Missouri Institute of Mental Health, University of Missouri-St. Louis, St. Louis, MO, USA

BACKGROUND

- Long COVID (LC) refers to symptoms that persist or emerge >3 months after SARS-CoV-2 infection.
- In this analysis of people with HIV (PWH) on stable antiretroviral therapy (ART), we examined whether:
  - HIV-related and neuropsychiatric (NP)-related parameters predicted the development of LC
  - NP parameter changes after COVID differed by LC status

METHODS

- RV254 Acute HIV Infection (AHI) cohort participants initiated and maintained ART from Fiebig stages I–V of AHI. They underwent regular NP assessments (see **Table 1**) during study visits at weeks 0, 24, 48, and every 48 weeks thereafter.
- Since 2020, COVID incidence was systematically recorded. Post-COVID symptoms were screened during study follow-up using a standardized checklist introduced in Jan 2022.
- Among those who have been on >48 weeks of ART, we compared their NP changes before and after 1st COVID, stratified by the presence of LC (i.e., LC+ vs. LC-).

Table 1. Neuropsychiatric Assessments

Mood Symptoms	Patient Health Questionnaire 9 (PHQ-9) Distress Thermometer (DT)
4-test Cognitive Battery	Color Trails 1 (CT1) Color Trails 2 (CT2) Trail Making A (TMT) Nondominant Grooved Pegboard Test (GPB)

RESULTS

Table 2. Participants' Characteristics at pre-COVID Assessment

	LC+ (n=60)	LC- (n=367)	p-value
Age, year	32.2 (28.6, 37.6)	32.3 (28.9, 38.0)	0.891
Male, n (%)	57 (95)	360 (98)	0.142
#HIV suppression, n (%)	60 (100)	363 (99)	0.416
Weeks post-AHI	335 (241, 383)	334 (237, 387)	0.888
CD4 T-cell count	657 (560, 781)	684 (567, 870)	0.391
CD8 T-cell count	600 (453, 760)	644 (486, 833)	0.178
CD4/CD8 ratio	1.22 (0.90, 1.35)	1.09 (0.88, 1.36)	0.307
z-CT1	1.32 (0.82, 1.92)	1.49 (1.04, 1.89)	0.243
z-CT2	1.05 (0.74, 1.65)	1.02 (0.56, 1.52)	0.260
z-TMT	1.00 (0.22, 1.44)	0.92 (0.32, 1.43)	0.948
z-GPB	0.77 (0.17, 1.19)	0.78 (0.09, 1.37)	0.935
***NPZ-4**	0.94 (0.62, 1.39)	1.01 (0.66, 1.30)	0.961
PHQ-9	5 (3, 7)	4 (1, 8)	0.108
DT	2.45 (1.00, 5.00)	2.10 (1.00, 4.10)	0.578

Median (Interquartile range) is provided unless specified. # Plasma HIV RNA <50 cps/ml; * NPZ-4: Average z-score of the 4-test battery.

We did not observe association between the development of long COVID and HIV-related or NP parameters at the pre-COVID assessment.

Individuals with long COVID showed less improvement on the Color Trails 2 and exhibited a greater increase in depressive symptoms over time.

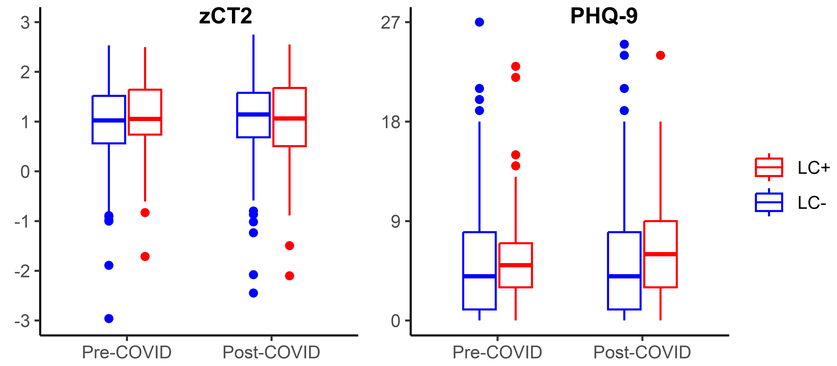


Table 3. Changes of Neuropsychiatric and HIV Metrics by Long COVID Status

	LC+ (N=60)		LC- (N=367)		
Outcome	**Pre-COVID**	**Post-COVID**	**Pre-COVID**	**Post-COVID**	**p**
z-CT1	1.32 (0.82, 1.92)	1.53 (0.97, 1.94)	1.49 (1.04, 1.89)	1.49 (1.08, 1.89)	0.948
z-CT2	1.05 (0.74, 1.65)	1.06 (0.48, 1.69)	1.02 (0.56, 1.52)	1.14 (0.68, 1.58)	**0.042**
Z-TMT	1.00 (0.22, 1.44)	0.90 (-0.21, 1.60)	0.92 (0.32, 1.43)	0.91 (0.39, 1.38)	0.235
z-GPB	0.77 (0.17, 1.19)	0.67 (0.22, 1.14)	0.78 (0.09, 1.37)	0.70 (0.14, 1.34)	0.500
NPZ-4	0.94 (0.62, 1.39)	0.97 (0.54, 1.38)	1.01 (0.66, 1.30)	1.03 (0.63, 1.37)	0.112
PHQ-9	5 (3, 7)	6 (3, 9)	4 (1, 8)	4 (1, 8)	**0.047**
DT	2.45 (1.00, 5.00)	2.25 (1.00, 5.30)	2.10 (1.00, 4.10)	2.00 (1.00, 4.20)	0.109
CD4 T-cell count	657 (560, 782)	687 (555, 818)	684 (567, 870)	680 (545, 871)	0.302
CD8 T-cell count	600 (453, 760)	629 (522, 770)	644 (486, 833)	649 (476, 841)	0.148
CD4/CD8	1.22 (0.90, 1.35)	1.15 (0.89, 1.30)	1.09 (0.88, 1.36)	1.08 (0.86, 1.35)	0.341

Medians (interquartile ranges) are presented. P-values were calculated to using the Wilcoxon rank-sum test to compare pre-/post-COVID changes between groups with and without long COVID (bolded for p<0.05).

Other Findings

- LC was observed in 14% (60/427) of participants.
- Neurologic symptoms (e.g., headache, insomnia, and cognitive and mood symptoms) were reported in 43% of LC+ individuals.
- Additional analyses of changes in cognitive performance using linear mixed models, adjusted for practice effects, yielded similar results (i.e., a significant difference in ΔCT2, p = 0.005).

SUMMARY OF KEY FINDINGS

- No association was observed between the development of LC and any HIV-related or NP parameters at the pre-COVID assessment (**Table 2**).
- Compared with the LC– group, the LC+ group showed less improvement on the CT2 test (**Table 3**). However, the actual differences in changes in z-CT2 between the LC+ and LC– groups were small and may not be clinically meaningful.
- Despite the absence of a statistical difference in PHQ-9 scores between the LC+ and LC– groups at the pre-COVID assessment, the LC+ group showed a greater increase in PHQ-9 scores at the post-COVID visit (**Tabe 3**). Further, up to one quarter of individuals with LC had PHQ-9 scores of potential clinical relevance (i.e., PHQ-9>9) at the follow-up visit.

LIMITATIONS

- RV254 participants were young, predominantly male, and mostly without chronic medical conditions other than HIV infection.
- Most COVID-19 incidents in RV254 were identified through participant self-report, lacking confirmatory PCR testing.
- Most of these COVID-19 events occurred during the Omicron surge periods or were associated with later Omicron-related variants.
- Correlation between long COVID status and vaccination was not explored due to the highly heterogeneous COVID-19 vaccination program in Thailand during the pandemic.

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DISCLAIMER

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