TRAJECTORY OF POST-COVID NEUROCOGNITIVE RECOVERY IN PEOPLE LIVING WITH AND WITHOUT HIV

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BACKGROUND

- It is unknown whether people living with HIV (PWH) and HIV-seronegative people have different neurocognitive symptoms or sequelae following COVID-19.
- A recent study in the LIINC cohort demonstrated that PWH are more likely to complain of neurocognitive symptoms post-COVID-19 than HIV-seronegative people.
- In the general population, brain fog and memory and concentration problems are highly reported after COVID-19.
- Here we used formal neurocognitive assessments at 1 and 4 months post-COVID-19 to objectively assess cognition in PWH and HIV-seronegative people post-COVID-19.
- Since HIV-Associated Neurocognitive Disorder (HAND) is experienced by 25-47% of PWH, we simultaneously assessed PWH and HIV-seronegative people who believed they never had COVID to determine whether differences in cognition associate with HIV or COVID-19.

CENTRAL QUESTION

- Are PWH more likely to score poorly on cognitive assessments in the post-acute phase of COVID-19 compared to HIV-seronegative people?

Table 1. Characteristics of 294 Cohort Participants Who Completed Neurocognitive Assessments

Characteristic	Arm 1, COVID+HIV+ (N=56)	Arm 2, COVID+HIV- (N=105)	Arm 3, COVID-HIV+ (N=66)	Arm 4, COVID-HIV- (N=67)
Age (years), median (IQR)	52 (38-59)	36 (26-48)	59 (51-64)	48 (36-62)
Sex, % (n)				
Male	86% (48)	35% (37)	61% (40)	39% (26)
Gender, % (n)				
Cisgender	91% (51)	97% (102)	95% (63)	100% (67)
Transgender	2% (1)	2% (2)	5% (3)	0% (0)
Other or Not Reported	7% (4)	1% (1)	0% (0)	0% (0)
Race, % (n)				
Asian	5% (3)	14% (15)	2% (1)	12% (8)
Black/African American	34% (19)	11% (12)	58% (38)	9% (6)
White	48% (27)	69% (72)	36% (24)	72% (48)
Multiracial or Not Reported	12% (7)	6% (6)	5% (3)	6% (5)
Ethnicity, % (n)				
Hispanic or Latino	21% (12)	5% (5)	9% (6)	9% (6)
Not Reported	0% (0)	1% (1)	0% (0)	3% (2)
Educational Level, % (n)				
Grades 1-8	7% (4)	0% (0)	0% (0)	0% (0)
Grades 9-11	0% (0)	0% (0)	12% (8)	3% (2)
Grade 12	13% (7)	3% (3)	18% (12)	3% (2)
Some College	29% (16)	10% (10)	35% (23)	12% (8)
Bachelor's	30% (17)	24% (25)	20% (13)	24% (16)
Graduate School	21% (12)	64% (67)	15% (10)	58% (39)
Income Bracket, % (n)				
<$25,000	38% (21)	10% (11)	65% (43)	16% (11)
$25,001-$50,000	18% (10)	13% (14)	14% (9)	7% (5)
$50,001-$80,000	18% (10)	10% (11)	11% (7)	9% (6)
$80,001-$130,000	4% (2)	21% (22)	6% (4)	13% (9)
>$130,000	16% (9)	37% (39)	2% (1)	48% (32)
Not Reported	8% (4)	8% (8)	4% (2)	6% (4)
Heavy Alcohol Use, % (n)	7% (4)	5% (5)	3% (2)	1% (1)
Recreational Substance Use, % (n)	46% (26)	19% (20)	29% (19)	16% (11)
COVID Vaccine Prior to Study Entry, % (n)	86% (48)	98% (103)	98% (65)	94% (63)
Body Mass Index, median (IQR)	27 (25-32)	25 (22-29)	27 (25-33)	26 (23-31)
Most Recent HIV Viral Load (copies/mL), % (n)				
Undetectable	82% (46)		91% (60)	
Lab CD4 Count cells/mm^3, median (IQR)	584 (346-754)		742 (509-976)	

STUDY METHODS

- 294 adult participants in the lower 48 United States were enrolled into four study arms between 6/14/2021 and 1/9/2023 and completed at least one cognitive assessment (Table 1, Figure 1).

- By using never-COVID controls, we show that the differences in neurocognitive scores between people living with HIV and HIV-seronegative people post-COVID are attributable to HIV and not to COVID.
- Separately, we show that processing speed is impaired 1 month post-COVID with recovery at 4 months post-COVID in vaccinated HIV-seronegative people.

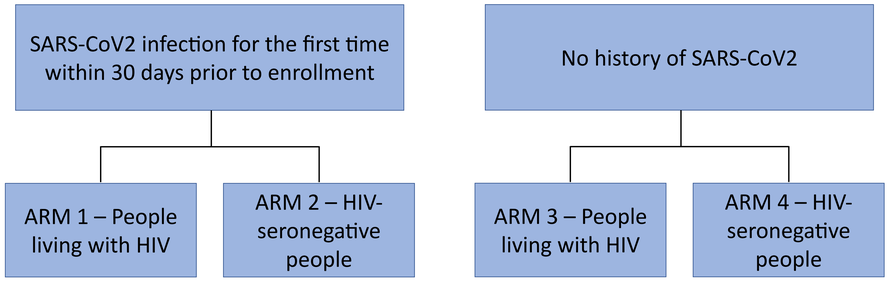


Figure 1. Cohort arms.

- Eleven cognitive assessments were administered by telephone at 1- and 4-months after COVID-19 symptom onset (post-COVID, arms 1-2) or 1- and 4-months post-enrollment (never-COVID, arms 3-4).
- The cognitive assessments included: Wechsler Adult Intelligence-IV (WAIS-IV) Information (IN); Hopkins Verbal Learning Test Revised (HVLT-R) for Verbal Learning (VL), Verbal Memory (VM), and Recognition Memory (RM); Oral Trail Making Test (OTMT) A and B; WAIS-IV Digit Span Forward (DSF) and Digit Span Backwards (DSB); Calibrated Ideational Fluency Assessment (CIFA) Verbal Fluency (VF) cued by letter and category.
- Standardized scores were generated using standard tables for each assessment, normalized by age. CIFA VF assessments were normalized for age, sex, and years of education.

- Differences in standardized scores between arms were analyzed using linear regression models adjusted for sex, education, and additional relevant demographic factors chosen with MANOVA. Differences in standardized scores between Month 1 and 4 were analyzed using paired t-tests.

RESULTS

- 1-month post-COVID, PWH scored lower than HIV-seronegative people in WAIS-IV IN and DSB, HVLT-R VM, and CIFA category-cued VF after adjustment for age, sex, years of education, and BMI. WAIS-IV IN was also adjusted for vaccination prior to COVID-19, and CIFA VF was also adjusted for race, income category, and recreational drug use.
- However, when comparing PWH at 1-month post-COVID to never-COVID PWH 1-month post-enrollment, *there were no significant differences* in all eleven cognitive assessments after the adjustments described above.
- Comparing HIV-seronegative people 1-month post-COVID to never-COVID HIV-seronegative people 1-month post-enrollment, post-COVID participants scored lower on OTMT-A ($p<0.01$) after adjustment for age, sex, years of education, BMI value, and recreational drug use.
- HIV-seronegative people scored higher at 4-months than at 1-month post-COVID on OTMT-A ($p<0.0001$), OTMT-B ($p=0.048$), DSF ($p=0.017$), and CIFA letter-cued VF ($p=0.012$).

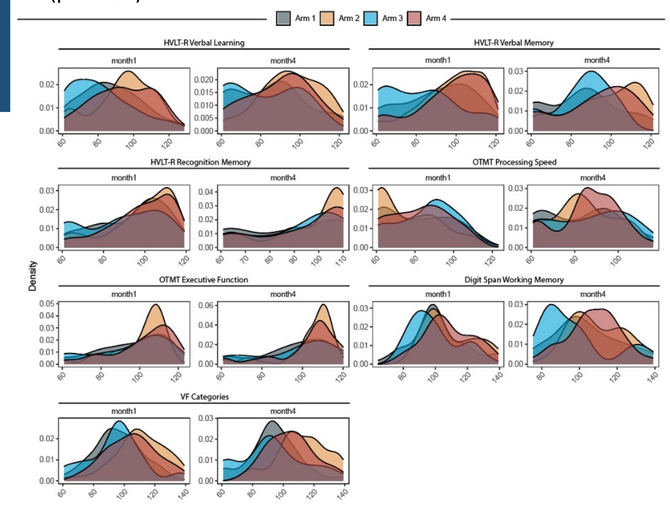


Figure 2. Distribution of age-standardized scores from the four study arms at 1 and 4 months post-COVID (arms 1 & 2) and post-enrollment (arms 3 & 4). CIFA VF scores are standardized by age, sex, and years of education.

CONCLUSIONS

- We show in a mostly-vaccinated cohort that the post-COVID differences in cognition between PWH and HIV-seronegative people post-COVID are attributable to HIV rather than COVID.
- Our results suggest that mental speed is impaired 1-month post-COVID with recovery at 4 months post-COVID in vaccinated HIV-seronegative people.

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