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Internalized HIV-Related Stigma and Neurocognitive Functioning Among Women Living with HIV

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Abstract

The prevalence of HIV-associated neurocognitive impairment persists despite highly effective antiretroviral therapy (ART). In this study we explore the role of internalized stigma, acceptance of negative societal characterizations, and perceptions about people living with HIV (PLWH) on neurocognitive functioning (executive function, learning, memory, attention/working memory, psychomotor speed, fluency, motor skills) in a national cohort of women living with HIV (WLWH) in the United States. We utilized observational data from a multicenter study of WLWH who are mostly African American living in low-resource settings. Neurocognitive function was measured using an eight-test battery. A multiple linear regression model was constructed to investigate the relationship between internalized stigma and overall neurocognitive functioning (mean of all neurocognitive domain standardized *T*-scores), adjusting for age, education, race, previous neuropsychological battery scores, illicit drug use, viral load, and years on ART. Our analysis revealed that internalized HIV-related stigma is significantly associated with worse performance on individual domain tests and overall neurocognitive performance ($B = 0.27$, $t = 2.50$, $p = 0.01$). This suggests HIV-related internalized stigma may be negatively associated with neurocognitive functioning for WLWH. This finding highlights a specific psychosocial factor associated with poor neurocognitive function that may be targeted to better promote the health of PLWH.

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Future research on the longitudinal relationship between these variables and the effects of other stigma dimensions on poor neurocognitive function would provide further insights into the pathways explaining the relationship between internalized stigma and neurocognition.

Keywords: HIV, stigma, neurocognitive function, cognitive decline, women, aging

Introduction

Although HIV-associated dementia has decreased due to highly effective antiretroviral therapy (ART), the prevalence of less severe HIV-associated neurocognitive impairment continues to increase.[1] Literature suggests that a majority of people living with HIV (PLWH) perform below expectations on formal neurocognitive evaluations and 50% of individuals receiving ART experience HIV-associated neurocognitive disorders (HAND), which can affect many neurocognitive domains, including motor skills, processing speed, executive functioning, and episodic memory.[2,3] Comorbid conditions and unsuppressed viral load may contribute to impairment but do not sufficiently explain the prevalence of impaired neurological functioning among ART-adherent PLWH.

Improved survival rates as a result of effective ART have shifted the disease burden to an older demographic. Older PLWH are at an increased risk of cognitive compromise, including reduced executive functioning, verbal and visual memory, and motor speed.[4] In turn, older PLWH with cognitive impairment are more prone to suboptimal medication adherence,[5] which results in lack of virologic suppression. In a cyclical fashion, unsuppressed viral load may, in turn, contribute to further impairment. Thus, it is critical to identify risk factors to attenuate cognitive decline and its consequences in this vulnerable population.

Cognitive decline can be observed globally, but it can also be observed in specific cognitive domains such as executive functioning (i.e., the ability to reason and problem solve), psychomotor speed (i.e., the ability to process information quickly), attention (i.e., the ability to focus), learning (i.e., the ability to acquire information), memory (i.e., the ability to retain information), fluency (i.e., verbal ability), and fine motor skills (i.e., the ability to physically manipulate objects).

Comparisons between men and women with HIV show a few cognitive differences, mostly with greater cognitive deficits observed in women, particularly in motor function, memory, and speed of information processing.[6] Differences in cognitive vulnerability observed in women living with HIV (WLWH) may stem from biological factors (e.g., hormonal, genetic) as well as systemic issues as many women are exposed to physical and sexual abuse, trauma, lower income and education, depression, and poorer health care utilization that compromises physical health, contributing to poorer brain health.[7,8]

In the Women's Interagency HIV Study (WIHS) in particular, these same seven cognitive domains have been assessed over time in those with and at risk for HIV.[9] Several trends have been observed. There are various heterogeneous cognitive profiles in which cognitive impairments are observed.[10] For example, in the WIHS virally suppressed WLWH have poorer global cognition compared with women without HIV, and this finding persists over time.

Further, virally suppressed WLWH are more likely to have poorer executive functioning and attention/working memory compared with women without HIV.[11] Interesting, stigma has not been examined as a predictor of cognitive function, but given the cognitive load in which stigma could exert on cognitive functioning, including it in such analyses is warranted.[12]

Stigma may be an underappreciated risk factor contributing to neurological decline among PLWH. Stigma is a social process by which individuals with perceived socially undesirable attributes or identities are viewed as socially less valuable than others.[13] Research suggests that HIV-related stigma is associated with suboptimal health behaviors and outcomes, including sub-optimal medication and HIV care visit adherence, poor mental health and social support, decreased trust in physicians, and poor viral suppression.[14–19]

There are several mechanisms through which HIV-related stigma has been negatively associated with neurocognitive functioning in PLWH. First, as a chronic stressor, stigma affects cerebrovascular risk,[14] neuroinflammation,[20,21] and the hypothalamic-pituitary-adrenal axis,[22,23] which can create neurobiological changes in the brain. Second, stigma can lead to depression.[24] Depression not only creates neurobiological changes in brain structures but also competes against other cognitive resources: If one is preoccupied by emotional concerns, fewer cognitive resources are available for other tasks, such as adherence to appointments and medications.[24,25]

Suboptimal adherence may then lead to viremia and ongoing inflammation, further impacting cognition. Stigma impacts the quantity and quality of social networks, which, in turn, is reflected in brain morphology.[26–31] Perceptions of stigma may lead PLWH to withdraw from social situations to avoid further stigmatization and/or unwanted disclosure of their HIV serostatus.[13,16] Stigma may also lead to substance use, which may have negative effects on the quality and quantity of social networks.[32]

These studies have demonstrated meaningful associations between HIV stigma and health through examination of different dimensions of stigma. Some have focused on anticipated stigma and its effect on health care behaviors, whereas others have hypothesized the role of internalized or experienced stigma on mental and physical health outcomes.

In this study, we sought to explore the role of internalized stigma, in particular, as a potential predictor of neurocognitive function. Internalized HIV-related stigma refers to PLWHs acceptance of negative societal characterizations and perceptions about PLWH and applying these to the self. Experienced stigma refers to differential treatment from others, anticipated stigma characterizes the expectation of enacted stigma, and internalized stigma describes the extent to which these negative attributes and beliefs are accepted internally.

Internalized stigma can limit social interactions and lead to dysphoria, decline in quality of life, social avoidance, delayed treatment response, and suboptimal treatment

adherence.[14,32–38] Internalized stigma is associated with decreased neurocognitive functioning among individuals suffering from mental illnesses such as schizophrenia.[39] To the best of our knowledge, however, the relationship between internalized HIV-stigma and neurocognitive function has not been examined, and only one study has examined the relationship between HIV-related experienced (not internalized) stigma and neurocognitive function, using a single-item, nonvalidated measure of stigma.[15]

In this study, we examine the association between internalized HIV-related stigma and neurocognitive functioning in a large cohort of WLWH using a reliable and valid multi-item measure of internalized HIV-related stigma. By investigating internalized stigma to determine whether it is significantly associated with neurocognitive functioning among WLWH, we hope to provide researchers, clinicians, and public health practitioners with a target so that intervention may be effectively employed to mitigate this pervasive modern morbidity.[40,41]

Methods

Participants and procedures

Data from October 16, 2017 to September 30, 2018 were extracted from the Women's Interagency HIV Study (WIHS).[42] The WIHS is the largest and oldest ongoing prospective cohort study of HIV among women in the United States with sites in Brooklyn, NY; Bronx/Manhattan; Washington, DC; Chicago, IL; San Francisco, CA; Chapel Hill, NC; Atlanta, GA; Birmingham, AL; Jackson, MS; and Miami, FL.[43–45]

The WIHS remains the leading study documenting the experience of WLWH in the United States due to its large sample size, collection of rich clinical, behavioral, and laboratory data, and large diverse biospecimen repository that spans more than 20 years. The WLWH enrolled in the study were demographically matched with HIV-negative controls with respect to demographic, behavioral, and other risk characteristics.

Participants in the neurocognitive assessments reflected similar race/ethnicity distributions (77% Black, 14% White, 13% Hispanic, 3% other) to that of WLWH in the United States (59% Black, 17% White, 19% Hispanic, 5% other).[46] Most participants in the study are poor, with 64% reporting an annual household income of $18,000 or less. Regarding education, 33% have attained less than a high school education. The WIHS is representative of the general population of women with HIV, with the significant exception that WIHS women are older, which makes them ideal subjects for study of neurocognitive decline. The average age of participants in our neurocognitive study was 50 years old.

Participants ($N = 803$) completed in-person visits during which trained staff administered assessments and questionnaires and collected blood samples. All participants provided informed consent, and the study protocols were approved by the respective Institutional Review Board (IRB) at each site and by the WIHS Executive Committee.

Neurocognitive assessments

The neuropsychological battery included eight tests: The Hopkins Verbal Learning Test-Revised (HVLT-R), Letter-Number Sequencing, Trail Making, Stroop Test, Symbol Digit Modalities Test (SDMT), Controlled Oral Word Association Test, Category Fluency Test (Animals), and Grooved Pegboard. Previous studies have demonstrated that this battery is a valid measure of neurocognitive functioning among PLWH, as they measure domains that are commonly assessed in HAND and are normed in the larger population.[46,47]

Seven domains were assessed using these tests: (1) executive function (outcomes = time to completion on Trail Making Test Part B and Stroop Test 3); (2) psychomotor speed (outcomes = total correct on SDMT, time to completion on Stroop Test 2); (3) attention (outcomes = total correct on Letter–Number Sequencing control and experimental conditions); (4) learning (outcome = total learning across HVLT-R trials); (5) memory (outcome = HVLT-R delayed recall); (6) fluency (outcomes = total correct on Controlled Oral Word Association Test and category fluency); and (7) fine motor function (outcomes = total time to completion for each hand on Grooved Pegboard).[11] Timed outcomes were log transformed to normalize distributions and reverse scored, so higher values indicated better performance.

Our analyses used *T*-scores (standardized) adjusted for age, education, race, and previous neurocognitive battery scores, which is consistent with previous large-scale cohort studies, including WIHS.[48–50] A composite *T*-score was derived by averaging *T*-scores for domains with more than one outcome. For domains with only one outcome, the outcome score was used as the domain score. For participants with scores on ≥4 domains, *T*-scores were also used to create a comprehensive (global) overall performance score.[51] Since the adjusted scores are derived internally, WIHS avoids bias associated with external norming, a factor that is particularly important for this cohort that is rich with diversity in race and socioeconomic environment and is made up entirely of women.[52]

Internalized HIV-related stigma

We used the negative self-image subscale of the revised HIV Stigma Scale,[53] which has been widely used in various ethnic/geographic populations and within the WIHS cohort.[38] The negative self-image subscale consists of 7 items, with a 4-point response scale (1 = strongly disagree to 4 = strongly agree). A sample item is ''I feel I'm not as good as others because I have HIV.'' Stigma scores were reflected by means of the scale items, and, therefore, the range was between 1 and 4. Higher scores on the stigma scale indicate more internalized stigma.

Covariates

Race, education level, time since ART initiation, and illicit substance use were self-reported. Viral load was measured as part of the WIHS, with undetectable viral load defined as <20 copies/mL versus detectable load defined as >20 copies/mL.[47]

Statistical analysis

To examine the factors associated with neurocognitive functioning, linear regression analyses were conducted. The primary independent variable was HIV-related internalized stigma; based on previous studies, we adjusted for a priori covariates, including time on ART, substance use, and viral load.[47] Note that domain *T*-scores were *already* adjusted for age, education, race, and scores on previous administration of the neurocognitive battery before analyses.

The seven domains of neurocognitive functioning were moderately correlated with each other, and Cronbach's alpha assessing internal consistency of the seven domains was 0.77 (based on the intercorrelations among the seven-domain means). Because of this relatively high alpha, we used overall neurocognitive functioning, the mean of standardized scores for the seven domains, as the outcome in our main analyses. A higher score in the overall variable as well as in each individual neurocognitive variable suggests better neurocognitive ability. Statistical analyses were performed using SPSS version 20 with a significance level of $p < 0.05$.

Results

Descriptive statistics for the sample are presented in Table 1. Bivariate correlations of internalized HIV-related stigma with the seven domains of neurocognitive functioning, as well as with overall neurocognitive functioning, are presented in Table 2. As can be seen, our analysis revealed that lower internalized HIV-related stigma was significantly associated with each of the seven individual domains of neurocognitive functioning (executive function, learning, memory, attention/working memory, psychomotor speed, fluency, and motor skills). Thus, lower internalized HIV stigma was significantly associated not only with individual subdomains of neurocognition but with overall neurocognitive functioning.

Table 1. Descriptive Statistics for the Study Sample ($N = 803$)

Variables	n *(%)*
Race/ethnicity	
Non-Hispanic White	72 (9.2)
Hispanic White	36 (4.6)
Non-Hispanic Black	586 (75.1)
Hispanic Black	16 (2.1)
Hispanic other	45 (5.8)
Other	25 (3.2)
Current illicit drug use	
Yes	149 (19.1)
No	630 (80.9)
HIV RNA viral load	
Detected	560 (69.7)
Undetectable	202 (25.2)
Variable, mean (SD)	
Age	50.44 (8.79)
Years on ART	13.03 (7.02)
Internalized HIV-related stigma	1.76 (0.65)
Overall neurocognitive functioning	3.65 (1.90)
Variable, mean (SD)	
Age	50.44 (8.79)
Years on ART	13.03 (7.02)
Internalized HIV-related stigma	1.76 (0.65)
Overall neurocognitive functioning	3.65 (1.90)
Executive function	48.64 (9.60)
Psychomotor speed	49.02 (9.54)
Attention	47.35 (9.51)
Learning	47.44 (10.41)
Memory	48.08 (10.59)
Motor function	49.92 (10.18)
Verbal fluency	48.76 (9.56)

Means are unadjusted values. Overall neurocognitive functioning ranges from 1 to 9.
ART, antiretroviral therapy; SD, standard deviation.

Table 2. Bivariate Correlations Between Internalized HIV-Related Stigma and Domains of Neurocognitive Functioning

Neurocognitive variables	r	p *(two-tailed)*
Overall cognitive functioning	–0.113[a]	0.001
Executive functioning	–0.115	0.001
Psychomotor speed	–0.075	0.034
Attention	–0.071	0.049
Learning	–0.134	0.000
Memory	–0.090	0.011
Motor	–0.071	0.044
Verbal	–0.083	0.019

[a]Overall cognitive functioning is the mean of all neurocognitive domain *T*-scores.

Similarly, a simple regression analysis yielded a significant association between internalized HIV stigma and worse overall neurocognitive functioning ($B = -0.33$, $t = -3.22$, $p = 0.001$). When entered into the regression model, none of the covariates were significantly associated with overall neurocognitive functioning (all p values >0.16), and the association between internalized stigma and worse overall neurocognitive functioning remained significant ($B = -0.27$, $t = -2.50$, $p = 0.01$).

Discussion

HIV-related stigma negatively affects health behaviors and outcomes among PLWH, especially women.[14–19] To the best of our knowledge, ours is the first study to describe a significant relationship between HIV-related internalized stigma and decreased neurocognitive functioning among PLWH. Findings also demonstrated significant negative associations between internalized stigma and specific neurocognitive domains such as executive functioning, psychomotor speed, attention, learning, memory, motor, and verbal skills.

The relationship between internalized HIV-related stigma and neurocognitive functioning has implications for future interventions; our findings highlight a specific predictor of neurocognitive decline that may be targeted by researchers, clinicians, and public health practitioners to protect and promote health among PLWH. By identifying PLWH with internalized HIV-related stigma, health care providers may have an opportunity to intervene and provide support for these individuals who may be at a heightened risk of neurocognitive decline, and, in turn, medication and care visit non-adherence.[5]

A variety of interventions have been developed to reduce internalized stigma,[54] several with promising effectiveness. Cognitive behavioral therapy aimed at modifying self-stigmatizing beliefs and psychoeducational interventions directed at stigma yielded promising results and may be adapted to improve both mental health and neurocognitive outcomes among PLWH.[55,56] With more than half of the HIV population older than 50 years,[57] and more vulnerable to neurocognitive decline than younger adults,[58,59] interventions addressing neurocognitive decline and associated risks are more important than ever.

In addition to psychoeducation interventions, building trust among WLWH and health care workers is another avenue for

reducing stigma. Previous studies have demonstrated significant associations between HIV stigma in the health care setting and lower trust in providers.[14,58] Community health workers may be an underutilized tool for mitigating this link.[59]

The limitations of our study suggest opportunities for further research. Due to the cross-sectional nature of the study design, the simultaneous assessment of independent variable and outcome precluded the delineation of a causal relationship between study variables. It is possible that neurocognitive decline may lead to more internalized stigma, rather than the reverse. It should be noted, however, that our measures of neurocognitive functioning are adjusted for previous administrations of neurocognitive measures.

We recommend long-term longitudinal studies examining the negative effects of internalized HIV-related stigma on neurocognitive functioning. Another limitation of our study is the demographic profile of our cohort, which consisted exclusively of WLWH enrolled in the WIHS. This limits the extrapolation of our findings to men living with HIV. Future studies should compare our findings with those of men with HIV; such comparisons may reveal potential differences in the magnitude and pattern of internalized stigma-associated neurocognitive decline.

The majority of participants in WIHS have received HIV treatment for numerous years. In addition, they are older than the national average for WLWH. Except these factors, WIHS participants are otherwise selected to be representative of the US population of WLWH. Finally, our stigma and neurocognitive scores are limited to our specific sample. Comparing the neurocognitive functioning of our sample with similar demographics, such as women not living with HIV, would be a useful target for further research.

Notwithstanding these limitations, this study contributes to a growing body of literature concerning the wide-reaching deleterious effects of HIV-related stigma in women living in low-resource settings. We encourage future research to examine the causal relationship between these variables and assess how internalized HIV-related stigma exacerbates neurocognitive decline. Future studies may also examine the effects of *intersectional stigma* (i.e., age-related stigma, racial stigma, sexual orientation stigma, etc.) as well as the mechanisms through which these effects are mediated.

In fact, as PLWH may be diagnosed with HAND and made aware of their cognitive impairments, this may create a new type of internalized stigma that could also impact neurocognition.[54] Finally, we hope this study can empower researchers and clinicians to explore the interventions designed to improve resilience to HIV-related stigma.[55,56]

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No competing financial interests exist.

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