Published in final edited form as:

Int J Geriatr Psychiatry. 2019 January ; 34(1): 72–78. doi:10.1002/gps.4988.

Resilience attenuates the association between neurocognitive functioning and everyday functioning in individuals aging with HIV in the Deep South

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Abstract

Objectives: Adults aging with HIV are at risk for poorer neurocognitive and daily functioning outcomes. Identifying factors to protect such outcomes is a significant research priority. The aim of this study was to explore the role of resilience in cognitive and everyday functioning in a largely African American and low socioeconomic status sample of adults and older adults with HIV in the Deep South.

Methods/Design: In this cross-sectional study 100 HIV+ middle-aged and older adults (range 40–73; 61% aged 50+) completed a comprehensive neurocognitive battery along with self-reported measures of resilience and everyday functioning.

Results: Higher resilience was associated with better global neurocognitive functioning ($\rho=0.31$, $p<0.01$), as well as better functioning in all domains (verbal fluency, executive functioning, speed of information processing, learning, working memory) except recall and motor skills. Resilience was also significantly associated with instrumental activities of daily living (IADL) dependence, with lower resilience observed in those with IADL dependence compared to those who were IADL independent ($p<0.01$). In a multiple regression adjusting for data-driven covariates (verbal IQ, income, depression), and global neurocognitive impairment, resilience was the only significant ($p=0.02$) correlate of IADL dependence. A follow-up mediation showed that the direct relationship between neurocognitive functioning and IADL declines was fully attenuated after accounting for shared variance with resilience.

Conclusions: Resilience is associated with better cognitive and functional outcomes in people aging with HIV. While further work is needed to understand these associations over time, results suggest interventions to build resilience may promote successful aging in this vulnerable population.

Keywords

resilience; HIV/AIDS; neurocognition; daily functioning

Introduction

The prevalence and incidence of HIV among older adults is growing due to decreases in mortality with antiretroviral therapy and an increase in new diagnoses in this age group. Estimates suggest that by 2020 70% of those living with HIV/AIDS in the U.S. will be aged 50 and above¹. Adults and older adults with HIV are at an increased risk for neurocognitive impairment (namely, HIV-associated neurocognitive disorder [HAND]) as a combined result of the effects of both aging as well as HIV disease². This neurocognitive impairment also puts this population at a higher risk for daily functioning impairments as well as poorer psychosocial and mental health outcomes^{3,4}. As such, it is crucial to identify ways to promote successful cognitive aging outcomes in this population as they reach older ages.

Positive psychological factors may be one area that may promote successful cognitive outcomes in older people living with HIV/AIDS (PLWHA). One such positive psychological factor is resilience. The American Psychological Association defines resilience as “the process of adapting well in the face of adversity, trauma, tragedy, threats, or significant sources of stress,” or “bouncing back” from difficult experiences⁵. Resilience is conceptually very similar to processes such as grit, post-traumatic growth, and optimism. This definition of a *process* versus a stable *personality trait* suggests that resilience is adaptive and that people have the capacity to build and improve resilience. In aging populations high resilience has been associated with positive outcomes, such as better mood and lower mortality risk, longevity, as well as higher self-rated successful aging, increased quality of life, and improved lifestyle behaviors⁶. Importantly, resilience can occur in diverse populations regardless of socioeconomic factors such as income, educational attainment, and race. In fact some evidence suggests that, minorities, particularly African Americans, may exhibit greater levels of resilience than their White counterparts⁷.

While research has traditionally focused on deleterious outcomes and risk factors associated with HIV, emerging research has begun to focus on both successful aging outcomes in this population as well as protective factors such as resilience. Qualitative work in individuals aging with HIV has suggested that indeed psychological strengths such as resilience and hardiness are reported in this population despite the challenges of aging with HIV^{8,9}. Quantitative studies have shown that while resilience levels may be lower in older PLWHA compared to their HIV-negative counterparts, adults aging with HIV/AIDS can still experience resilience and successful aging in spite of the deleterious effects of the disease^{10,11}. Resilience has been shown to predict health-related quality of life in a recent large (N=335) study of older gay and bisexual men¹². Another recent study by Moore et al. examined successful cognitive aging (operationally defined as freedom from cognitive, everyday, and emotional impairments) in older PLWHA, and found that resilience did not differ between HIV-negative individuals defined as successful or unsuccessful cognitive agers, while it did between those HIV-positive persons who were defined as successful vs

unsuccessful cognitive agers¹⁰. This suggests that resilience may be particularly protective for promoting successful aging outcomes in those with HIV. Another study showed that higher self-rated successful aging (using a 10-point scale) in older PLWHA had a stronger association with positive psychological traits such as resilience, optimism, and sense of personal mastery than duration or severity of HIV disease¹¹, which is promising given that resilience may be a malleable intervention target. Resilience may reduce the negative influence of life stress on physical, emotional, and functional/global well-being in older PLWHA¹³, as has been demonstrated in normal aging¹⁴.

Very few studies have examined the association between resilience and neurocognitive outcomes specifically in individuals aging with HIV. Another recent study from our group examined the conceptually similar construct of grit (i.e., perseverance/passion for goals and maintenance of effort and determination despite obstacles¹⁵) and showed that adults with HIV (range 36–65, mean age = 50.54) had lower grit scores than HIV-uninfected adults, and grit was associated with better neurocognitive and daily functioning in the HIV-positive sample but not in the HIV-negative sample¹⁶. Similarly, findings from the aforementioned Moore et al.¹⁰ study suggest that positive psychological factors may be particularly influential on successful cognitive aging in older PLWH as compared to HIV-negative counterparts. While several studies show that traditional proxies for cognitive reserve, such as education level and verbal IQ, are predictive of cognitive outcomes in HIV-infected individuals, these factors don't fully account for all of the variability in functioning. As a result, recent work has modified operational definitions of cognitive reserve to include non-cognitive factors such as positive psychological factors, including resilience,^{15,17,18} and such factors have been referred to as reserve capacity^{19,20}. In the current study, we examined the role of resilience as a potential “psychological reserve” factor¹⁶ that may influence cognition and everyday functioning among individuals with HIV.

Given the aging of the HIV population, their heightened risk for neurocognitive and functional impairments, and the evidence that resilience is not only possible in this population—but that it may promote better outcomes, research on this potentially modifiable psychological factor is warranted. The aim of the current study was to gain a further understanding of the role of resilience in cognitive and everyday functioning outcomes in a largely African American and low socioeconomic status (SES) sample of adults and older adults (age range 40 to 73; 61% aged 50+) with HIV living in the Deep South. Those few studies that have examined this topic have been in largely White male samples, which may not generalize to African American populations. Indeed, the Deep South has emerged as an epicenter of HIV/AIDS, with a large prevalence of HIV/AIDS among African Americans of low SES^{21,22} who may be particularly at risk for development of HAND^{23,24}.

Materials and Method

Participants and Procedure

One hundred HIV+ individuals were recruited from a local HIV/AIDS clinic (see Table 1 for sample characteristics). A brief telephone screen determined eligibility, which included the following: aged 40+, HIV+, no conditions that may affect neurocognitive functioning (e.g., Schizophrenia, Alzheimer's disease), not blind or deaf, no head injury with loss of

consciousness longer than 30 minutes, and not currently undergoing chemo or radiation therapy. While age 50 is often used as the cutoff in studies pertaining to aging-related issues in people living with HIV, the current study employed a 40+ cutoff for several reasons: 1) the prevalence of HAND is higher in middle-aged and older PLWH than their younger counterparts, 2) using a younger cutoff allowed more variability in age to examine in analyses, 3) given that cognitive declines in fluid abilities may begin in the 40's in PLWH, examining correlates of cognitive and functional outcomes from a life course perspective may be advantageous, particularly with regard to identifying early indicators of decline and implications for interventions. After completing the IRB approved consent form, enrolled participants completed a comprehensive neurocognitive battery and several self-reported questionnaires, including everyday functioning and depressive symptoms. Participants returned for a second day of testing to complete additional questionnaires pertaining to successful aging, including the resilience questionnaire. Table 1 includes sample characteristics.

Measures

Resilience.—The Connor-Davidson Resilience Scale-10 was used to measure resilience in the current study²⁵. This 10-item measure contains items such as *“I can deal with whatever comes my way”*, and responses are on a Likert scale ranging from 1 (*not true at all*) to 5 (*true nearly all of the time*). Items are summed for a total score, with higher scores reflecting greater levels of resilience. The internal consistency in the current study was high (Cronbach's $\alpha = 0.90$).

Neurocognitive functioning.—Participants completed a comprehensive neurocognitive battery commonly used in the HIV literature³. Test scores were corrected for age, education, gender, and race/ethnicity when available and then used to calculate global and domain T-scores (verbal fluency, executive function, speed of information processing, learning, recall, working memory, motor). In order to derive neurocognitive impairment, global T-scores were transformed into clinical ratings using a validated algorithm consistent with the current nosology for HAND diagnoses for research purposes²⁶. Clinical ratings of five or greater was used to define neurocognitive impairment. T-scores and neurocognitive impairment were both examined in analyses.

Everyday functioning.—Everyday functioning was assessed via two self-report questionnaires commonly used in HIV^{3,27,28}. Instrumental activities of daily living (IADL) declines were assessed using a revised version of the Lawton, Brody²⁹ everyday functioning questionnaire^{3,27}, in which participants rate their current functioning compared to prior functioning across 12 activities (e.g., housekeeping, managing finances, managing medications, shopping, cooking, transportation, understanding written material/television). In this study, two indices were examined: total number of IADL declines continuous score (possible range: 0–12) as well as IADL dependence (2 declines operationalized as “IADL dependent”).

The second everyday functioning measure used in this study was the 34-item Patient's Assessment of Own Functioning Inventory (PAOFI), which captures perceived cognitive

symptoms in daily life across several domains (e.g., language and communication [example item: “How often do you have difficulty thinking of the names of things?”]; higher level cognitive and intellectual function [example item: “How often do your thoughts seem confused or illogical?”])³⁰. Responses are on a Likert scale (*Almost always, Very often, Fairly often, Once in a while, Very infrequently, and Almost never*) and items reported as *Fairly Often* or greater were defined as “significant” cognitive symptoms. Thus the total score for the PAOFI reflects the number of significant everyday cognitive symptoms (possible range: 0–34).

Covariates.—We considered the following covariates: age, sex/gender, race/ethnicity, education level, and income, all gathered via a demographic questionnaire. HIV characteristics were derived from clinic records and included current and nadir CD4 count as well as plasma viral load. We also examined depressive symptoms as measured by the Center for Epidemiological Studies Depression Scale (CES-D)³¹ as well as verbal IQ (a commonly used proxy for cognitive reserve in this population³²) as measured by the Wide Range Achievement Test (WRAT) 4th Edition – reading subtest³³.

Results

Resilience was not associated with age, education, race, gender, current or nadir CD4, or plasma viral load in our sample of adults and older adults with HIV. Higher resilience was associated with greater income ($\rho=0.33$, $p<0.001$), less depressive symptoms ($\rho=-0.48$, $p<0.001$), and higher WRAT scores ($\rho=0.26$, $p<0.01$). Regarding cognitive and functional outcomes, higher resilience was associated with better global neurocognitive functioning ($\rho=0.31$, $p<0.01$), as well as better functioning in the domains of verbal fluency ($\rho=0.21$, $p=0.04$), executive functioning ($\rho=0.28$, $p<0.01$), speed of information processing ($\rho=0.24$, $p=0.02$), learning ($\rho=0.21$, $p=0.04$), and working memory ($\rho=0.22$, $p=0.03$), but was not significantly related to the domains of recall or motor skills. Resilience was also significantly associated with global neurocognitive impairment, such that those with cognitive impairment had lower levels of resilience ($F(1,98)=10.10$, $p<0.001$; cognitively impaired $M(SD)=36.08$ (8.32), normal cognition= 40.67 (5.77)). Lastly, lower resilience was univariately associated with IADL declines ($\rho=-0.27$, $p<0.01$), IADL dependence ($F(1,97)=7.34$, $p<0.01$; dependent $M(SD)=35.45$ (8.18), independent= 39.70 (6.89)), and more cognitive symptoms (i.e., PAOFI total scores; $\rho=-0.27$, $p<0.01$). In a multiple regression model predicting global neurocognitive impairment, higher resilience remained significantly associated with less impairment ($p=0.03$) after adjusting for variables associated with resilience and neurocognitive impairment (WRAT, income, and depressive symptoms) (Table 2). Similarly, when IADL dependence was the outcome, with the aforementioned covariates plus global neurocognitive impairment, resilience remained significant ($p=0.02$) and was the only significant predictor in the model (Table 2).

Given this prior analysis and the correlations between resilience and functional outcomes (IADL and PAOFI), we were interested in formally testing whether the association between neurocognitive functioning and everyday functioning traditionally reported in the literature would be mediated by resilience. First we determined whether cognitive symptoms or IADL declines were associated with neurocognitive functioning (global T-scores), and found that

greater IADL declines were associated with lower global T-scores ($p=0.04$). Cognitive symptoms were unassociated with global T-scores ($p=0.44$). Then, given the association between neurocognitive functioning and IADL declines, we conducted a mediation analysis using the Barron and Kenny³⁴ approach to test whether the association between global neurocognitive performance and IADL declines would be mediated by resilience. As previously reported, for Step 1, global T-scores were inversely associated with IADL declines ($\beta=-0.21$, $p=0.04$). For Step 2, as previously reported, global T-scores were positively associated with resilience ($\beta=0.30$, $p<0.01$). For Step 3, when resilience and global T-scores were included in the same model predicting IADL declines, resilience was associated with IADL declines ($\beta=-0.25$, $p=0.02$), while global T-scores were not ($\beta=-0.13$, $p=0.19$). Thus, the direct relationship between neurocognitive functioning and IADL declines were attenuated after accounting for shared variance with resilience (Figure 1).

Discussion

As hypothesized, resilience was related to neurocognitive performance, and more specifically neurocognitive impairment, among adults and older adults living with HIV. This effect remained after considering confounders, including demographics, cognitive reserve, and depressive symptoms. Similarly, resilience was significantly related to everyday functioning impairment, above and beyond global neurocognitive impairment. In fact, the relationship between worse cognitive functioning and greater IADL declines was weakened when associations between these factors and resilience were taken into account.

These data provide cross-sectional evidence that declines in neurocognition may lead to lower resilience, which in turn may lead to worse daily functioning. Alternatively, it may be that those who are more resilient are better able to compensate for cognitive declines, and are thus less affected by these declines on everyday functioning. This point is very significant in HIV; as numerous studies have highlighted the importance of cognitive functioning in predicting daily functioning in this population³. However, research has also shown cognitive deficits are not necessarily the strongest predictor of functional declines among the HIV population, but that functional ability is related to a myriad of factors (i.e., depressed mood^{3,35}, substance use³⁶, and apathy³⁷) in addition to cognition. While we did find that those with more depressive symptoms had lower levels of resilience, in our models predicting both global cognitive impairment and IADL dependence, resilience was still significant even when taking into account depression. This highlights the strong and independent effect of resilience on cognitive and everyday outcomes. Perhaps resilience may buffer some of the deleterious effects of depression on such outcomes.

Few studies have considered psychological non-cognitive reserve variables, such as resilience, in relationships with cognitive and everyday functioning in individuals with HIV. The current study complements the limited studies in HIV suggesting that factors such as grit and resilience are associated with better cognitive and everyday outcomes¹⁶. These findings support the notion that indeed expanding traditional proxies for cognitive reserve to include non-cognitive psychological reserve factors may aid future research in gaining a better understanding of successful cognitive aging.

Furthermore, bolstering resilience may provide a way to improve or protect both cognitive and everyday functioning outcomes. Albeit, it may be possible that boosting resilience may yield a positive effect on daily functioning without necessarily being via the mechanism of improving cognition.

There is a large body of research on psychosocial and positive psychology interventions³⁸. A recent large systematic review on such interventions in PLWH showed little to no effects on depression, anxiety, stress, and coping. Interestingly, none of the studies included in this review integrated the concept of resilience into the intervention content³⁹. Despite the emerging interest in resilience, relative to other psychosocial and mental health targets such as depression, fewer intervention studies have targeted the construct of resilience. Those studies that do exist target two distinct populations with specific goals: 1) those who have already experienced some specific type of non-normative trauma (e.g., military servicemen, victims of natural disasters) with the goal of targeting resilience to achieve an end goal (e.g., alleviating post-traumatic stress disorder), and 2) building resilience in clinical (e.g., diabetes) and non-clinical populations (e.g., corporate settings, college students) with the goal of preparing individuals for future generalized life stressors^{40–42}. The only known intervention study targeting resilience in HIV examined a resilience intervention in PLWH in rural China, and showed promising results on depression and resilience⁴³. The core resilience framework focused on positive reframing, healthy activities, social connections, and coping, which offers insights for future resilience interventions in PLWH. Similarly, a resilience curriculum grounded in the Transactional Model of Stress and Coping and the Protective Factor Model of Resilience has shown efficacy in African Americans with type-2 diabetes in improving resilience as well as distal outcomes including clinical diabetes markers (e.g., fasting glucose)^{44,45}. This may be particularly relevant to PLWH as it suggests that resilience interventions may improve proximal psychological (e.g., depressive symptoms) and HIV self-management (e.g., ART adherence) outcomes, which may ultimately improve distal functional (e.g., cognitive function) and HIV outcomes (e.g., CD4 count). Much more work is needed to develop and test resilience interventions targeted for individuals aging with HIV.

Strengths of the current study include the examination of an understudied yet significant topic in HIV+ adults and older adults using a well-validated resilience measure as well as a comprehensive neurocognitive battery and commonly used cognitive reserve proxy (WRAT). Further, the current sample was largely African Americans of low SES, which in this case represents a strength as it allows for comparisons for prior studies examining this topic in a different HIV demographic. Limitations include cross-sectional design, and lack of an HIV-negative control group. Future longitudinal studies are needed to better understand resilience across the lifespan in individuals aging with HIV, including examining resilience as a predictor of future cognitive and functional declines as well as the underlying mechanisms in which resilience may protect these outcomes. Furthermore, understanding the impact of HIV on resilience throughout the course of the disease is important. Specifically, while some may perceive the stress of an HIV diagnosis as a traumatic event, several studies have suggested that in a subset of PLWH, living with an HIV diagnosis may be perceived in a positive light and promote sources of strength^{8,9}. Future observational studies may benefit from utilizing real-time data, such as ecological momentary assessment (EMA), which may

be especially beneficial in examining the potential buffering role of resilience on time-lagged relationships between neurocognitive ability, depressed mood, and everyday functioning. Furthermore, such methods may be particularly useful in intervention studies in determining their efficacy in real-time contexts as well as mechanisms of action. Given that HIV infection is now considered a manageable chronic disease, bolstering resilience in this population just as in non-pathological aging persons may prepare this population for future stressful life experiences—both disease related and not.

Acknowledgements & Funding:

This study was funded by NIH/NIMH (1R01MH106366–01A1; Vance, P.I.) and NIH/NIA (R00AG048762; Fazeli, P.I.). The research was conducted via the NIH/NIA Edward Roybal Center (5P30AG02283814). Dr. Fazeli is also supported by L30AG045921. The authors have no conflicts of interest to disclose.

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Key Points:

- Individuals aging with HIV are at greater risk for cognitive and functional impairments than their non HIV-infected counterparts
- Determining protective factors to promote successful aging in this population is warranted; resilience may represent one such factor
- Resilience was associated with better neurocognitive and everyday functioning, even when accounting for mood, socioeconomic, and cognitive reserve factors
- Resilience attenuated the association between neurocognitive functioning and everyday functioning, suggesting that this psychological factor may be particularly a beneficial intervention target for buffering the negative effects of neurocognitive impairment on everyday outcomes

a= association between independent variable and mediator

b= association between mediator and outcome variable

c= association between independent variable and outcome variable

c'= association between independent variable and outcome variable when mediator is in the model

Figure 1.
Mediation Model

Table 1.**Sample Characteristics (N=100)**

Variable	M (SD) or %
Demographic Characteristics	
Age (years) (range 40—73)	51.73 (7.01)
Sex, % male	59%
Education (years)	12.50 (1.83)
Race/Ethnicity, % Black	84%
Yearly Income	
\$0–\$10,000	56%
\$10,001–\$20,000	29%
\$20,001–\$30,000	9%
\$30,001–\$40,000	4%
\$30,001–\$40,000	2%
Resilience	
Connor Davidson Resilience Scale-10	38.28 (7.54)
Neurocognitive Variables	
Verbal IQ (WRAT)	89.91 (14.66)
Global Neurocognitive T-score	45.08 (5.73)
Verbal Fluency Mean T-score	46.45 (7.81)
Executive Functioning Mean T-score	46.07 (8.22)
Speed of Information Processing Mean T-score	47.68 (8.12)
Learning Mean T-score	43.33 (6.87)
Recall Mean T-score	44.31 (6.89)
Working Memory Mean T-score	45.34 (8.90)
Motor Mean T-score	40.17 (9.48)
% with Global Neurocognitive Impairment	52%
Everyday Functioning	
IADL Declines	1.53 (2.19)
% with IADL Dependence	33%
Everyday Cognitive Symptoms	7.77 (8.08)
Depressive Symptoms	
Center for Epidemiological Studies-Depression Scale	18.01 (10.74)
HIV Disease Characteristics	
Current CD4 (cells/ul)	695.53 (385.14)
Nadir CD4 (cells/ul)	258.94 (271.47)
Plasma viral load detectability, % undetectable	68%

Note. N for Current CD4=75, Nadir CD4=96, plasma viral load detectability=81

Table 2.

Multiple Regression Estimates

Variables	Dependent Variable: Neurocognitive Impairment			Dependent Variable: IADL Dependence		
	B(SE)	Lower 95% CI	Upper 95% CI	B(SE)	Lower 95% CI	Upper 95% CI
Income	-0.31 (0.27)	-0.87	0.16	-0.15 (0.25)	-0.72	0.27
WRAT	-0.02 (0.02)	-0.06	0.01	0.00 (0.02)	-0.03	0.04
CES-D	0.02 (0.02)	-0.07	0.03	-0.03 (0.02)	-0.07	0.02
Resilience *	-0.08 (0.04)	-0.16	-0.01	-0.09 (0.04)	-0.17	-0.02
Neurocognitive Impairment	--	--	--	-0.09 (0.25)	-0.58	0.39

Note.

* p<0.05;

WRAT=Wide Range Achievement Test; CES-D=Center for Epidemiological Studies-Depression Scale