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Risk Factors of Cognitive Decline in Older Caregivers With HIV: An Emerging Hypothesis

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Abstract

People with HIV (PWH) are living longer and healthier lives; thanks to combination antiretroviral therapy. As many PWH age, they find themselves providing care to family members and friends, just as their counterparts without HIV. The literature indicates that becoming a caregiver creates conditions that compromise one's cognitive function. Additionally, nearly 45% of all PWH experience HIV-associated neurocognitive disorder and are already vulnerable to cognitive impairment due to HIV, aging, and accompanying health conditions, and lifestyle factors. Given what is known, we assert that caregivers with HIV, especially as they age, are at additional risk for developing cognitive impairments. The purpose of this commentary was to briefly examine the juxtaposition between cognitive vulnerability of caregiving and the cognitive vulnerability of aging with HIV. Potential factors contributing to impaired cognition include stress, lack of social support, stigma, lifestyle, and comorbidities. Implications for clinical practice and research are provided.

Key words: caregiver, care recipient, social support, stress, cognitive deficits, HIV-associated neurocognitive disorder, dementia

In the United States, nearly 50% of people with HIV (PWH) are aged 50 years old or older (Centers for Disease Control and Prevention, 2019); by 2030, this is projected to be 70% (Smit et al., 2015). Due to effective combination antiretroviral therapy (cART), PWH can expect to live healthier and longer lives (Waldrop et al., 2021). As such, instead of being recipients of care, as PWH age, they are in position to provide care to family members and/or friends. It is reasonable to assume that many PWH are already providing care to their own children and/or grandchildren, but others may also be providing care to an ill or aging family member, partner,

or friend, which has its own unique caregiving burden profile (Lee et al., 2021). To our knowledge, there are no official numbers of caregivers with HIV. Of the 1.2 million adults with HIV in the United States (Centers for Disease Control and Prevention, 2021), it was estimated that more than 140,000 of these individuals are caregivers with HIV, and of these, it is likely that more than 50% of caregivers with HIV are older than 50 years (Lee et al., 2021); for comparison, in the general U.S. population, about 35.9% of the population is 50 years and older (US Census Bureau, 2021).

From a cognitive perspective, PWH providing care is concerning for two reasons: (a) caregivers, in general, are vulnerable to cognitive impairment (Corrêa et al., 2019; Vitaliano et al., 2017) and (b) PWH are more vulnerable to cognitive impairment compared with those without HIV (Waldrop et al., 2021). The purpose of this commentary was to briefly examine the juxtaposition between cognitive vulnerability of caregiving and the cognitive vulnerability of aging with HIV. We hypothesize that caregivers with HIV, especially those who are older, will be at an increased risk for developing cognitive impairments, which is driven by several factors. Hypothetical case examples of caregivers with HIV are provided. Finally, implications for clinical practice and research are posited.

Caregivers and Cognitive Vulnerability

Many health care professionals may be surprised that informal caregivers are susceptible to developing

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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cognitive impairments. Informal caregivers experience long-term burden and stress related to aspects of caregiving, such as the frequency and severity of care-recipient symptoms, assisting with activities of daily living, and social isolation (Kim et al., 2012). Such unique stressors activate the hypothalamic–pituitary–adrenal axis, which increases glucocorticoids (stress hormones, such as cortisol) that can be neurotoxic and neuroinflammatory to the brain (Corrêa et al., 2019). The prolonged secretion of these stress hormones can decrease cognitive reserve (Cody & Vance, 2016). Also, the act of caregiving itself can be socially isolating; such social isolation and accompanying loneliness exerts a negative impact on cognitive reserve and brain health (Boss et al., 2015; Lara et al., 2019).

Although research on the relationship between caregiving and cognitive function has been contradictory, with some finding that cognition may be protected in caregivers (O’Sullivan et al., 2019), the preponderance of evidence suggests that caregiving places many caregivers at risk for cognitive impairments relative to non-caregiving peers. For example, in a national representative survey (i.e., English Longitudinal Study of Ageing) of 4,117 caregivers and 4,793 noncaregivers, García-Castro et al. (2021) found that caregivers experienced higher levels of executive function and memory problems compared with noncaregivers. Similarly, in a sample of 122 spousal dementia caregivers and 117 demographically matched noncaregivers (both without HIV) followed over 2 years, Vitaliano et al. (2017) found that the dementia caregivers reported more subjective cognitive problems and more objective cognitive decline than the noncaregivers.

This cognitive vulnerability in caregivers is affected by care recipient characteristics (e.g., disruptive behaviors) and caregiver lifestyle factors (e.g., comorbidities, sleep) known in the cognitive aging literature to affect cognitive reserve (Waldrop et al., 2021). Similarly, in a study of 527 dementia caregivers compared with 527 demographically matched controls from a normative database, Lathan et al. (2016) found that dementia caregivers performed worse on measures of memory and information processing speed. Further analysis showed that poorer sleep, less perceived social support, more years of caregiving (when interacting with education level), and being non-White were associated with poorer cognitive function. Other studies have found similar predictors of cognitive impairment in caregivers, including care recipient hyperactivity (De Vugt et al., 2006), subjective caregiver competences (De Vugt et al., 2006), poor sleep (Brewster et al., 2021), health behaviors (García-Castro et al., 2021), depression (García-

Castro et al., 2021; Vitaliano et al., 2017), stress exposure (Corrêa et al., 2019; Vitaliano et al., 2017), chronic burden (Brigola et al., 2017), and frailty of the caregiver (Brigola et al., 2017). Caregivers with HIV share many of these vulnerabilities as well.

HIV and Cognitive Vulnerability

Since the beginning of the HIV epidemic, the cognitive vulnerability of PWH has been well-documented, ranging from cognitive complaints to dementia (Waldrop et al., 2021; Wei et al., 2020). With advances in cART yielding more potent, durable, and tolerable treatment for HIV, today the severe impact of HIV on the brain has decreased substantially with fewer than 2% of PWH experiencing HIV-associated dementia (Wei et al., 2020). Yet, the pervasive cognitive vulnerability of PWH is still demonstrated by approximately 44.9% of PWH meeting the clinical criteria for HIV-Associated Neurocognitive Disorder (HAND).

To diagnose HAND, causes of cognitive impairment unrelated to HIV, such as major depressive disorder, heart disease, renal disease, liver disease, hypertension, Alzheimer disease, and other comorbidities, must be excluded. Yet, as people age with HIV, they can experience many of these comorbidities. In fact, these comorbidities may be exacerbated by HIV, which can then have a synergistic impact on cognitive reserve and brain health (Hobkirk et al., 2017; Vance et al., 2013; Waldrop et al., 2021).

The stress of stigma (i.e., stigma related to HIV, aging, race, homophobia, and their intersection), social withdrawal/loneliness, depression/anxiety, poverty, food insecurity, housing insecurity, and medical management of HIV and other comorbidities can create chronic stress that activates the “flight or fight” physiological response to stress (Cody & Vance, 2016; Slater et al., 2015; Stadtler et al., 2021; Vance et al., 2013). Overactivation of the stress response can create a cumulative burden that can damage the body (Picard & McEwen, 2018). This burden, referred to as allostatic load, is often measured by a sum of cardiovascular, neuroendocrine, and inflammatory biomarkers (e.g., interleukin 6, tumor necrosis factor alpha). Fazeli, Waldrop-Valverde, et al. (2020) found that higher allostatic load was associated with poorer cognitive functioning in a sample of PWH 50 years old or older. This is particularly concerning given that a systematic review of 66 studies (Lowther et al., 2014) found that PWH disproportionately experience stigma (42–83%), loneliness (46%), anxiety (21–40%), and depression (34–42%), which can affect cognitive functioning via

several direct and indirect pathways, including increasing allostatic load.

Older Caregivers With HIV and Cognitive Vulnerability

Older caregivers with HIV will likely have increased risk of developing cognitive impairment compared with older noncaregivers with HIV, older noncaregivers without HIV, and older caregivers without HIV. Moreover, PWH have a higher prevalence in some types of disease, such as diabetes mellitus and cardiovascular disease, which have been suggested to contribute to cognitive decline (Frison et al., 2021; Song et al., 2020). What is certain is that there are some overlapping risk factors that may be exacerbated from being both a caregiver and living with HIV, including social support, stress, and poor medical management.

Social support and social connectedness are essential in maintaining the health of caregivers, with such social contact reducing loneliness and providing cognitive stimulation (Vance, 2013; Vance et al., 2019), as well as providing physical support in the caregiving duties (Li et al., 2021); however, caregiving itself can be isolating, resulting in limited opportunities for social connectedness (Li et al., 2021). Such social isolation may be especially impactful for older caregivers with HIV; HIV stigma (and other intersecting stigmas) can hinder social connectedness (Vance et al., 2019), which may already be limited when providing care to someone. For many older caregivers with HIV who have not disclosed their HIV status or sexual identity to family members or friends, reaching out to these same people for social support during caregiving may be difficult for fear that such information may be revealed or the discovery of such information may be met with disapproval or even alienation or hostility.

Stress is another factor that clearly overlaps with caregiving and aging with HIV. PWH experience a low-grade inflammatory response to HIV, even in the context of controlled virus, which is known to contribute to poorer brain health and poorer cognition (Waldrop et al., 2021). The aggregate impact of both aging with HIV (e.g., stigma) and caregiving burden (e.g., financial pressure, social isolation) can increase stress responses, sometimes expressed as depression and anxiety; increased depression and/or anxiety stimulates the hypothalamic–pituitary–adrenal axis, exacerbating allostatic load that can be damaging to the brain and the immune system.

Medication management (e.g., keeping medical appointments, adhering to medication regimens)

represents another area in which both caregivers and PWH experience difficulties. For example, in a sample of 45 informal caregivers of people with dementia, Wang et al. (2015) found that nearly half had problems keeping their scheduled medical appointments, and nearly a third missed doses of their medication occasionally or frequently. Caregiving to others, thus, can ironically compromise self-care and long-term health of the caregiver. In the HIV literature, missed HIV clinic appointments and missed medications are common problems and are associated with poor health outcomes (Fazeli, Wood, et al., 2020). For older caregivers with HIV, caregiving may exacerbate difficulty adhering to HIV medical treatment and treatment for HIV comorbidities (e.g., heart disease, hypertension). Furthermore, if cART is missed, this can lead to viral resistance over time. HIV is regarded as a “slow burner” inflammatory disease; such inflammation can create neuroinflammation that damages the brain. Studies show that if cART is initiated and maintained, the detrimental impact of this inflammation is partially minimized (Zhuang et al., 2017). Thus, by skipping doses of cART, this places PWH at additional risk of suffering cognitive decline.

Hypothetical Case Scenarios

It is likely that some caregivers with HIV have more resources (e.g., cognitive reserve, income) and coping strategies to buffer the challenges and mitigate these cognitive vulnerabilities better than others. To illustrate these complexities, two hypothetical cases are provided.

Hypothetical Case 1

Barney, a White, 67-year-old, disabled, gay man has been living with HIV since his early 40s. Unfortunately, he was diagnosed late when the disease had already progressed to AIDS; however, after receiving cART, his immune system eventually reconstituted, allowing him to live with only minor HIV-related complications. For 12 years, he has been living with his partner Darrell, a Black, 71-year-old, retired engineer. Two years ago, Darrell was diagnosed with mild cognitive impairment that quickly progressed to Alzheimer disease. The transition to dementia was marked by: (a) a need to monitor Darrell throughout the day due to increasing behavioral symptoms of dementia; (b) reduction in Barney's exercise routine, skipping his medical appointments, and forgetting to take his own medications; (c) Barney's increased depression over the situation and difficulty coping; and (d) friends avoiding visits with the couple because it was uncomfortable seeing both Darrell and

Barney this way. Barney would ask his family for help, but they are already estranged due to Barney's "homosexual lifestyle." The interracial stigma around their partnership complicated Barney's relationship with his family even more. Barney is concerned about his financial circumstances because he and Darrell are not legally married; the house is in Darrell's name, and most of the household income comes from Darrell's retirement, not from Barney's disability.

There are many risk factors that may affect Barney's cognition. First, his health status is at-risk, especially concerning the management of his HIV. Second, his depression, lack of social support, increased social isolation, caregiving-related stress, and financial concerns are stress-producing, which can stimulate the hypothalamic–pituitary–adrenal axis that over time can compromise his brain health. Without intervention, Barney's current situation could increase his chances of developing cognitive decline.

Hypothetical Case 2

Fred, a Black, 66-year-old straight man and retired elementary school teacher, was diagnosed with HIV in his early 30s. Diagnosed early, he immediately received cART, which allowed him to live relatively free of any major HIV-related complications. For the past 15 years, he has been living with his wife Georgina, a White, 64-year-old, retired high school principal. Three years ago, Georgina had a stroke, leaving her cognitively impaired with difficulty walking. The transition was problematic for both, especially for Fred because he took on the caregiving duties and all aspects of managing the household. During this time, Fred sought the support they both needed. Fred, with the help of a social worker, had a ramp installed to help Georgina ambulate into and out of the house more easily. Also, Fred retained respite and adult daycare services, allowing time in his schedule for self-care needs such as attending his medical appointments, picking up his and Georgina's medications, and socializing with friends. During this time, their friends and family have been supportive in visiting because it is difficult for Fred and Georgina to leave the house. Fred realizes the situation is not ideal, but is appreciative of all the support.

Cognitive risk factors that accompany older caregivers with HIV, such as stigma, lack of social support, and poor self-care, although present, are mitigated in this hypothetical case. Fred has the financial and social resources to advocate for what he and Georgina need. By being proactive to address their needs, Fred was able to potentially reduce the stress and protect his cognitive health.

Implications for Clinical Practice and Research

As alluded to above, Lee et al. (2021) identified several themes associated with older caregivers with HIV that need to be researched and addressed in clinical practice: (a) adjusting to the caregiving role, (b) caregiving responsibilities, (c) HIV health care, (d) other health issues, (e) support systems, (f) resilience, and (g) stigma. Approaches to addressing the needs of older caregivers with HIV should begin by focusing on these themes to reduce stress, increase knowledge, provide social support and social interaction, and help maintain self-care behaviors that promote health. For example, programs to improve resilience may be an approach to use with this group. In a sample of 14 older PWH, Fazeli et al. (2021) delivered a resilience program composed of a 3-hr group session with quizzes, videos, and written activities. Participants overall found it highly acceptable (8.71 out of 10) and recommended that it address stigma, disclosure concerns, treatment adherence, and health concerns, which are overlapping themes among caregivers with HIV.

Addressing strategies to protect and promote cognitive health in older PWH, including those caregivers with HIV, should also be a focus. Vance et al. (in press) provided several areas in which to address cognitive vulnerability in older PWH; these include: (a) cART adherence to maintain viral control, (b) treatment of comorbidities such as diabetes and heart disease to avoid the negative impact on brain health and cognition, (c) treatment of neuro-comorbidities such as depression, (d) treatment of substance misuse to mitigate their impact on brain health and cognition, (e) mindfulness approaches to reduce stress, (f) cognitive training to support existing cognitive functioning, and (g) general health promotion (i.e., sleep, physical activity).

Conclusion

Given the impact of stress and lack of self-care associated with caregiving on the caregiver's health, older caregivers with HIV are cognitively vulnerable and are at increased risk of additional cognitive impairment. This intersection between the caregiving and the neuro-cognitive HIV literature becomes more complicated when considering the effect that COVID has on brain health, social connectedness, and social well-being of PWH and older PWH (Vance et al., 2021). The themes mentioned in this article merely highlight some of the germane areas that will require our attention as nurses, physicians, social workers, psychologists, and policy makers.

Disclosures

None.

Author Contributions

All authors on this article meet the four criteria for authorship as identified by the International Committee of Medical Journal Editors (ICMJE); all authors have contributed to the conception and design of the study, drafted or have been involved in revising this manuscript, reviewed the final version of this manuscript before submission, and agree to be accountable for all aspects of the work. Specifically, using the CRediT taxonomy, the specific contributions of each author is as follows: Conceptualization: D. E. Vance, Y. Lee, D. S. Batey, F. Puga, O. J. Clay, J. Y. Byun, A. R. Long, M. Rafford, C. Xiao, and P. L. Fazeli; Investigation: D. E. Vance, Y. Lee, D. S. Batey, F. Puga, O. J. Clay, J. Y. Byun, A. R. Long, M. Rafford, C. Xiao, and P. L. Fazeli; Project Administration: D. E. Vance, Y. Lee, D. S. Batey, F. Puga, O. J. Clay, J. Y. Byun, A. R. Long, M. Rafford, C. Xiao, and P. L. Fazeli; Writing—Original Draft: D. E. Vance, Y. Lee, D. S. Batey, F. Puga, O. J. Clay, J. Y. Byun, A. R. Long, M. Rafford, C. Xiao, and P. L. Fazeli; Writing—Review & Editing: D. E. Vance, Y. Lee, D. S. Batey, F. Puga, O. J. Clay, J. Y. Byun, A. R. Long, M. Rafford, C. Xiao, and P. L. Fazeli.

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