



HHS Public Access

Author manuscript

J Assoc Nurses AIDS Care. Author manuscript; available in PMC 2025 August 13.

Published in final edited form as:

J Assoc Nurses AIDS Care. 2024 ; 35(6): 519–529. doi:10.1097/JNC.0000000000000491.

Emotional Loneliness is Related to Objective Cognitive Function in Older People With HIV in the Washington-Baltimore Area: A Cross-Sectional Study

Moka Yoo-Jeong, PhD, RN^{*} [Assistant Professor],

School of Nursing, Bouvé College of Health Sciences, Northeastern University, Boston, Massachusetts, USA

Raha M. Dastgheyb, PhD [Assistant Professor],

Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

Eran F. Shorer, MD, MSc [Postdoctoral Research Fellow],

Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

Cornelia Demsky, BA [Senior Research Coordinator],

Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

Olivia Fox, BS, BA [Research Program Director],

Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

Divya Inaganti [undergraduate student],

Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

Sarah Kanner, BS [Clinical Research Program Coordinator],

Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

Ava G. Neijna, BA [Clinical Research Assistant],

Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

^{*}Corresponding author: Moka Yoo-Jeong: m.yoo-jeong@northeastern.edu.

Author Contributions

All authors on this paper 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 & Methodology: M. Yoo-Jeong, L. Rubin, T. Wilson; Formal Analysis: L. Rubin, R. Dastgheyb, E. Shorer; Funding acquisition: L. Rubin; Investigation: L. Rubin; Project administration: C. Demsky, O. Fox, D. Inaganti, S. Kanner, A. Neijna; Supervision: L. Rubin; Validation: L. Rubin, T. Wilson; Writing – original draft: M. Yoo-Jeong; Writing/Revising – L. Rubin, T. Wilson.

Disclosure Statement

The authors report no real or perceived vested interests that relate to this article that could be construed as a conflict of interest.

Alison Buchholz, PhD [Assistant Professor],

Department of Neurology, Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

Tracey E. Wilson, PhD [Distinguished Service Professor],

Department of Community Health Sciences and Vice Dean for Faculty Affairs and Research, Downstate Health Sciences University, Brooklyn, New York, USA

Leah H. Rubin, PhD, MA, MPH [Professor]

Department of Neurology, Department of Psychiatry and Behavioral Sciences, Department of Molecular and Comparative Pathobiology, Johns Hopkins University School of Medicine, Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA.

Abstract

Loneliness confers a significant risk to numerous health outcomes including cognitive impairment. This study assessed the relationship between loneliness subtypes (social and emotional) and cognition in older people with HIV (OPWH aged 50). Forty-two participants (mean age = 61.5 years; 48% male; 74% Black) completed the 6-item De Jong Gierveld Loneliness Scale and measures assessing objective and subjective cognition and depressive symptoms (Patient Health Questionnaire [PHQ-9]). Loneliness-cognition associations were examined using linear regression. Models were first adjusted for age, sex, race, and education, and then PHQ-9 score. Mean emotional and social loneliness scores were 1.24 (SD = 1.22) and 1.21 (SD = 1.14), respectively. After sociodemographic and PHQ-9 adjustment, emotional, but not social, loneliness was associated with poorer objective cognitive performance on processing speed (Digit Symbol) and executive function (CalCAP™). Findings have potential clinical importance for interventions that target specific loneliness subtypes to optimize cognitive performance in OPWH.

Keywords

emotional loneliness; loneliness; objective cognition; older persons with HIV; social loneliness; subjective cognition

Loneliness, defined as the feeling of being isolated that stems from a perceived deficit in social connections (Hawkey & Cacioppo, 2010), is a transdiagnostic construct that co-occurs with and exacerbates a range of mental, physical, and cognitive complications (Käll et al., 2020). Loneliness affects health outcomes either directly or indirectly through a cascade of biological and behavioral changes that are detrimental to health (Cacioppo et al., 2014). Loneliness has often been conceptualized as consisting of at least two subtypes, which are positively associated with one another but which may have unique contributions to different health and quality of life outcomes (Weiss, 1975). Emotional loneliness refers to the perceived absence of a close, intimate relationship. Conversely, social loneliness is related to the perceived absence of a desired social network that provides a sense of belonging and community (Manoli et al., 2022; Weiss, 1975). A number of studies have demonstrated that emotional and social loneliness are only moderately correlated, which

indicates that they are distinct with unique underlying features (Wolters et al., 2023). These dimensions may be independently associated with cognitive outcomes.

Several longitudinal cohort studies demonstrate that loneliness, using an unidimensional measure of loneliness, increases the risk for dementia (Salinas et al., 2022; Sundström et al., 2020; Sutin et al., 2020). There is emerging evidence in the general population of older adults that the two subtypes of loneliness may have different effects on cognition. In people with mild to moderate dementia, social, but not emotional, loneliness was associated with poorer language skills (Carbone et al., 2022). In addition, a longitudinal study conducted using the Health and Retirement Survey found that older adults with cognitive impairment experience higher levels of overall emotional and social loneliness compared to those without cognitive impairment, even after controlling for factors such as physical health, depressive symptoms, and marital status (Lee et al., 2022). This study also found that for men, higher emotional loneliness was related to dementia status, while this was not the case for women.

A rapidly growing population of individuals at risk for loneliness and cognitive impairment is older persons with HIV (OPWH aged 50 years). It is projected that this age group will represent as many as 73% of people with HIV (PWH) in the United States by 2030 (Smit et al., 2015). Notably, more than half of OPWH in clinical studies report significant loneliness (Greene et al., 2018; Harris et al., 2020; Yoo-Jeong et al., 2020). OPWH are at risk for premature and accelerated cognitive aging due, in part, to brain atrophy or accelerated cortical tissue loss (Becker et al., 2011), greater multimorbidity burden at a younger age (Hosaka et al., 2019), viral-mediated changes in the immune system (Hong & Banks, 2015; Rubin et al., 2020), and/or initial brain injury very early in the course of HIV infection (Valcour et al., 2011). The deleterious effects of loneliness on cognition parallel those associated with HIV and aging, underscoring the pressing need to investigate the effects of loneliness on cognitive function among OPWH.

There are a few published research studies demonstrating a relationship between loneliness and objective cognition in OPWH. In a cross-sectional study of 856 Canadians with HIV (mean age = 53, SD = 8.3), greater loneliness was associated with poorer global cognition (Harris et al., 2020). Another cross-sectional study at the Rush Center of Excellence on Disparities in HIV and Aging found an interaction effect of self-identified race and emotional loneliness on cognition in OPWH, such that the relationship between greater loneliness and lower global cognitive was found only in OPWH who identify as Black or African American, but not among Whites (Han et al., 2017). Despite the emerging evidence on the independent role of loneliness subtypes on cognition in the general older adult population without HIV, there is a gap in understanding the relationships of emotional and social loneliness on both subjective and objective cognitive performance in this clinical population that are at increased vulnerability to cognitive deficits. As such, our study sought to explore the relationships of overall, social, and emotional loneliness with both subjective and objective cognition in a sample of OPWH. Assessing the relationships of loneliness subtypes on cognitive function in OPWH can be valuable in designing targeted interventions specific for its adverse sequelae on cognitive function.

Methods

Participants and Data Collection

OPWH from the Johns Hopkins Center for the Advancement of HIV Neurotherapeutics clinical cohort were included in our current analysis. Data were collected from March 2021 to June 2022. Participants in the clinical cohort were primarily recruited through the John G. Bartlett HIV Practice at Johns Hopkins Hospital and from the surrounding Baltimore community. Participants were older than 50 years, able to provide written informed consent, on antiretroviral therapy, and could ambulate to the clinic for assessments. Participants were excluded if they had a history of opportunistic central nervous system infection, psychosis, or chronic central nervous system neurologic disorders defined via self-report and/or were an active substance abuser defined as any illicit history of illicit drug use within three months preceding the study visit (except for marijuana). Active substance use was established by subjective history and urine toxicology screens. Participants provided written informed consent and then completed measures of loneliness, objective and subjective cognitive function, reading ability, mental health, and functional assessments. All participants also had a blood draw as part of the our study for CD4 and viral load measures. Participants were compensated for their travel and time. The Institutional Review Board of the Johns Hopkins University approved the study (NA_00004930).

Measures

Loneliness.—We used the De Jong Gierveld Loneliness Scale, a 6-item questionnaire measuring overall, emotional, and social loneliness (De Jong Gierveld & Kamphuls, 1985; Gierveld & Tilburg, 2006). On this scale, first three items assess emotional loneliness (e.g., *I often feel rejected*) and the last three items assess social loneliness (e.g., *There are many people I can trust completely*). Response options for each item include: *yes, more or less, or no*. For the negatively worded emotional loneliness items (items 1–3), the neutral and positive responses are scored as 1. Specifically, *yes* = 1, *more or less* = 1, and *no* = 0. The total score ranges from 0 to 3 with higher scores equating to more emotional loneliness. For the positively worded social loneliness items (items 4–6), the neutral and negative responses are scored as 1. Specifically, *yes* = 0, *more or less* = 1, and *no* = 1. Again, the total score ranges from 0 to 3 with higher scores equating to greater social loneliness. For both emotional and social loneliness subscales, scores of 1–3 are considered lonely. Overall loneliness is then computed as the sum of the two subscales (scores range from 0 to 6), with a score of ≥ 2 indicating lonely individuals. In the current study, internal consistency of the emotional and social loneliness subscales scores was good (emotional loneliness: $\alpha = 0.72$; social loneliness: $\alpha = 0.79$; overall scale: $\alpha = 0.70$) and was comparable to other studies of similar age groups (45–64 years of age; emotional loneliness: $\alpha = 0.69$; social loneliness: $\alpha = 0.78$; overall scale: $\alpha = 0.73$) (Gierveld & Tilburg, 2006).

Cognition.—*Objective Cognition:* a neuropsychological test battery was used to objectively assess cognitive function across multiple cognitive domains. *Learning and memory* was assessed with the Hopkins Verbal Learning Test (Benedict et al., 1998) and Rey-Osterrieth Complex Figure Test (Rey, 1941). *Verbal fluency* was assessed with the Controlled Oral Word Association Test (Benton, 1968) and Animal Fluency. *Motor skills*

were assessed with the Grooved Pegboard™ Test (Reitan R. & Wolfson, 1985). *Processing speed* was measured with the Trail Making Test Part A (Reitan R. & Wolfson, 1985), the Digit Symbol Test (Wechsler, 1981), and Stroop color and word trials. *Executive function* was assessed with the Trail Making Test Part B (Reitan R. & Wolfson, 1985) and Stroop-interference. *Attention/working memory* was assessed with the California Computerized Assessment Package (CalCAP)™ (Miller et al., 1991), which includes tests of information processing and reaction times (simple, choice, sequential). All timed measures were log transformed and reverse scored so that higher log transformed scores indicate better performance across all objective measures. For all other tests, the outcome measures used for analysis were the raw test scores.

Subjective Cognition.: Subjective measures of cognitive function included three questionnaires: Cognitive Failures Questionnaire (Broadbent et al., 1982; Rast et al., 2009), a 25-item measure assessing forgetfulness and distractibility; Behavior Rating Inventory of Executive Function-Adult Version-includes nine clinical subscales to measure executive functioning and self regulation (Roth, Isquith, & Gioia, 2005). We used inhibit, monitor, set-shift, working memory, and planning and organization scales to assess executive dysfunction; and Barrett Impulsiveness Scale (Patton et al., 1995), a 30-item scale used to measure impulsivity. Higher scores on each of these scales/subscales equated to more subjective cognitive complaints.

Covariates were selected based on previous findings that suggest an association with cognition in people with HIV and included sociodemographic factors (e.g., age, biological sex, race and ethnicity, and years of education), reading ability (using the Hopkins Adult Reading Test (Schretlen et al., 2009)), CD4+ T cell count, HIV viral suppression (suppressed < 20 cp/ml vs not suppressed 20 and < 100 cp/ml), and depressive symptoms ([PHQ]-9)(Kroenke et al., 2016). We examined these factors in relation to loneliness and cognitive outcomes and those identified as covariates (associated with loneliness and cognition) were included in the adjusted models.

Data Analysis

Descriptive statistics were used to calculate the means and standard deviations of the continuous variables and the percentage and frequency of the categorical variables. Pearson's correlations were initially conducted to assess the unadjusted associations between loneliness subtypes (emotional, social, overall) and cognition (objective and subjective). Next, hierarchical multivariable linear regressions were conducted to determine the association between loneliness and each cognitive outcome (objective and subjective). The first series of analyses focused on the relationship between overall loneliness and cognition (objective and subjective). Block 1/Model 1 included the following sociodemographic covariates: age, sex, race, and education. Block 2/Model 2 included the same sociodemographic variables as in Model 1 with the addition of overall loneliness. For each cognitive outcome (objective and subjective), we assessed the proportion of variance explained by the covariates in Model 1 followed by the additional variance explained by adding overall loneliness into the model. Subsequent analyses were conducted to ensure that the relationships between overall loneliness and cognition were not accounted for

by depressive symptoms (PHQ-9). Model 1 variables were sociodemographics. Model 2 added the PHQ-9 total scores. Then, Block 3/Model 3 added overall loneliness. A similar series of analyses were conducted to determine the association between loneliness subtypes and cognition. Emotional and social loneliness subscale scores were included in the same block of the analysis given that the correlation between subscale scores was 0.19 ($p = .23$). We performed additional analyses with sociodemographics in Model 1, PHQ-9 in Model 2, and loneliness subtypes in Model 3 for each cognitive outcomes. Analyses were performed using IBM SPSS Statistics 29.0 and R version 4.3.1 with significance set at $p < .05$. No adjustments were made for multiple testing as the analyses were conducted for heuristic purposes to illustrate the potential clinical significance of loneliness as an important contributor to cognition.

Results

Descriptive Statistics

Forty-two OPWH with well-controlled HIV (mean age = 61.5 [SD = 6.7]; 48% men; 74% Black and non-Hispanic; mean years of education = 13.3 [SD = 2.6]) completed the De Jong Gierveld Loneliness Scale and objective neuropsychological and subjective cognitive assessments. Mean score on the overall loneliness scale was 2.45 (SD = 1.82); emotional and social loneliness subscales were 1.24 (SD = 1.22) and 1.21 (SD = 1.14), respectively. An overview of the descriptive statistics and average scores on the study variables are presented in Table 1.

Overall Loneliness and Cognition

After adjusting for sociodemographic variables, greater overall loneliness was associated with poorer performance on letter fluency, Trail Making Test Part A, Grooved Pegboard™ Test non-dominant hand, CalCAP™ sequential minus simple, and Digit Symbols (see Table 2). Greater overall loneliness was also associated with all of the subjective measures of cognition (p 's < 0.05). After additional adjustment for depressive symptoms (Table 3), overall loneliness remained significantly associated with letter fluency and Grooved Pegboard™ Test non-dominant hand ($\beta = 0.33$, $p < .05$ and $\beta = 0.39$, $p < .05$, respectively) as well as with greater subjective complaints on the Behavior Rating Inventory of Executive Function inhibit and set-shifting subscales ($\beta = 0.34$, $p = .03$ and $\beta = 0.36$, $p = .01$, respectively). Similarly, there was a significant R^2 change in these cognitive outcomes above and beyond depressive symptoms.

Emotional and Social Loneliness and Cognition

After adjusting for sociodemographic variables, emotional, but not social, loneliness was associated with poorer performance on letter fluency, Digit Symbol, Trail Making Test Part A, Trail Making Test Part B, Stroop-interference, and CalCAP™ sequential minus simple (Table 2). Both emotional and social loneliness were related to the majority of subjective cognitive outcomes when only sociodemographic covariates were adjusted in the models. The relationship between loneliness subscales and subjective cognition became non-significant after adjusting for depressive symptoms (Table 3). After further adjustment for depressive symptoms, the relationships between emotional loneliness remained with

performance on Digit Symbol and CalCAP™ sequential minus simple ($\beta = 0.34, p < .01$ and $\beta = 0.39, p < .05$, respectively).

Discussion

The aim of the current study was to explore whether overall, emotional, and social loneliness have differential relationships with objective and subjective cognition in a population of OPWH. In covariate controlled analyses, we found that both overall and emotional loneliness were related to several objective measures of cognition, while social loneliness was not. After accounting for depressive symptoms, neither emotional nor social loneliness were associated with subjective measures of cognition.

Our findings show that higher overall loneliness is related to poorer performance on several objective neuropsychological measures, which is consistent with previous studies in the general population of older adults (Salinas et al., 2022; Sundström et al., 2020; Sutin et al., 2020) and among those with HIV (Harris et al., 2020). Our results also suggest there are differential associations of loneliness subtypes with objective cognition, such that emotional loneliness, but not social loneliness, is associated with some measures of processing speed (e.g., Digit Symbol, Trail Making Test Part A), verbal fluency (letter fluency), and executive function (CalCAP). Significant association between emotional loneliness and processing speed (Digit Symbol) and executive function (CalCAP) remained even after further adjusting for depressive symptoms, which gives implications that emotional loneliness is related to specific domains of cognitive performance above and beyond the influence of depressive symptoms. This is important given that the majority of extant literature uses a single dimension of loneliness in relation to cognitive functioning. Emotional loneliness stems from a perceived deficiency in intimate social relationships or impaired social cognition (Gardiner et al., 2018). Thus, while initiatives aimed at fostering social interactions can address social loneliness, these strategies may not effectively mitigate emotional loneliness and its potential adverse effects on cognition. As such, intervention efforts that target emotional loneliness are needed.

While social loneliness was related to some subjective measures of cognition, it was not related to any of the objective measures of cognition when sociodemographics were controlled for. Significance went away when depressive symptoms were adjusted for, implying that subjective cognition is mainly associated with depressive symptoms and that social loneliness has limited influence on objective and subjective cognition altogether. Previous research in older adults without HIV suggests that emotional loneliness, rather than social loneliness, is more strongly associated with health indices including mortality and mental health outcomes (Dahlberg & McKee, 2014; Hyland et al., 2019; O'Suilleabháin et al., 2019). Our results support these findings that, while social loneliness is important to consider, emotional loneliness may be the driving factor to objective cognitive health and thus it is important to distinguish loneliness subtypes when examining cognitive function.

The Evolutionary Theory of Loneliness (Cacioppo et al., 2014) posits that loneliness affects cognition via health behaviors and biological mechanisms. Extant studies among the general populations demonstrate that loneliness is associated with several biological pathways,

including, but not limited to, increased pro-inflammatory markers (Hackett et al., 2012), activation of the hypothalamic-pituitary-adrenal-axis (Hawkley et al., 2012), and higher cortisol levels (Doane & Adam, 2010) that are linked with cognitive function. It might be that emotional loneliness may be directly related to these underlying physiological markers and/or disrupted neural circuits (Finley & Schaefer, 2022; Lam et al., 2021), which may have subsequent implications on cognition and overall health. As such, future research should consider elucidating biological or neural mechanisms explaining the contribution of emotional loneliness on cognition, as well as characterizing biomarkers that may be directly related to each loneliness subtype. In addition, as loneliness is a modifiable factor, interventions aimed at reducing loneliness may be helpful in improving specific cognitive domains, but to our knowledge, no studies have investigated these interventions and further studies are needed.

There are limitations to consider when interpreting our findings. Our cross-sectional design precludes inferences about causality. Our small sample size limits generalizability of the findings and may not have detected sufficient power for findings. The small sample size also prevented us from conducting post hoc analysis to assess for potential moderating or mediating effects of depressive symptoms in the findings. Generalizability may be limited since our sample was predominately recruited from one geographic location. Finally, although the measure we used to assess for loneliness subtypes has been validated and has showed good internal consistency within our sample, it is worth noting that the use of negatively and positively worded items for emotional and social loneliness subscales, respectively, may have introduced a potential source of bias and influenced our results (Penning et al., 2014).

Despite study limitations, our findings, examined within the context of a well-characterized sample, suggest that loneliness subtypes are differentially associated with cognitive outcomes among OPWH, which have implications for future research. To identify the potential mechanisms of these relationships our findings require replication within larger samples and the utilization of longitudinal approaches to gain perspective on causal relationships between loneliness subtypes and cognition.

Conclusions

Our findings provide preliminary evidence that loneliness subtypes may have different effects on cognitive outcomes among OPWH. Based on our findings, it is important to distinguish between emotional and social dimensions of loneliness in research on cognition among OPWH. Future research employing longitudinal designs, larger sample sizes, and identifying potential mechanisms is needed to confirm directionality and causality of the relationship between emotional loneliness and cognitive function among OPWH. This evidence would help inform future interventions in this high priority population at risk for loneliness.

Acknowledgements

This work was supported by the Johns Hopkins University Center for the Advancement of HIV Neurotherapeutics (JHU CAHN; P30MH075673, MPI: Rubin, Slusher, Clements) and the National Institute of Mental Health

(R01MH128955, MPI: T. Wilson, J. Meyers). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

References

- Becker JT, Sanders J, Madsen SK, Ragin A, Kingsley L, Maruca V, Cohen B, Goodkin K, Martin E, Miller EN, Sacktor N, Alger JR, Barker PB, Saharan P, Carmichael OT, & Thompson PM (2011). Subcortical brain atrophy persists even in HAART-regulated HIV disease. *Brain Imaging and Behavior*, 5(2), 77–85. 10.1007/s11682-011-9113-8 [PubMed: 21264551]
- Benedict RHB, Schretlen D, Groninger L, & Brandt J (1998). Hopkins Verbal Learning Test—revised: Normative data and analysis of inter-form and test-retest reliability. *The Clinical Neuropsychologist*, 12(1), 43–55. 10.1076/clin.12.1.43.1726
- Benton AL (1968). Differential behavioral effects in frontal lobe disease. *Neuropsychologia*, 6(1), 53–60. 10.1016/0028-3932(68)90038-9
- Broadbent DE, Cooper PF, FitzGerald P, & Parkes KR (1982). The Cognitive Failures Questionnaire (CFQ) and its correlates. *The British Journal of Clinical Psychology*, 21(1), 1–16. 10.1111/j.2044-8260.1982.tb01421.x [PubMed: 7126941]
- Cacioppo JT, Cacioppo S, & Boomsma DI (2014). Evolutionary mechanisms for loneliness. *Cognition & Emotion*, 28(1), 3–21. 10.1080/02699931.2013.837379 [PubMed: 24067110]
- Carbone E, Piras F, Pellegrini FF, Caffarra P, & Borella E (2022). Individual differences among older adults with mild and moderate dementia in social and emotional loneliness and their associations with cognitive and psychological functioning. *BMC Geriatrics*, 22(1), 859. 10.1186/s12877-022-03517-2 [PubMed: 36380269]
- Dahlberg L, & McKee KJ (2014). Correlates of social and emotional loneliness in older people: Evidence from an English community study. *Aging & Mental Health*, 18(4), 504–514. 10.1080/13607863.2013.856863 [PubMed: 24251626]
- De Jong Gierveld J, & Kamphuis F (1985). The development of a Rasch-type loneliness scale. *Applied Psychological Measurement*, 9(3), 289–299. 10.1177/014662168500900307
- Doane LD, & Adam EK (2010). Loneliness and cortisol: Momentary, day-to-day, and trait associations. *Psychoneuroendocrinology*, 35(3), 430–441. 10.1016/j.psyneuen.2009.08.005 [PubMed: 19744794]
- Finley AJ, & Schaefer SM (2022). Affective neuroscience of loneliness: Potential mechanisms underlying the association between perceived social isolation, health, and well-being. *Journal of Psychiatry and Brain Science*, 7(6), e220011. 10.20900/jpbs.20220011 [PubMed: 36778655]
- Gardiner C, Geldenhuys G, & Gott M (2018). Interventions to reduce social isolation and loneliness among older people: An integrative review. *Health & Social Care in the Community*, 26(2), 147–157. 10.1111/hsc.12367 [PubMed: 27413007]
- Gierveld JDJ, & Tilburg TV (2006). A 6-item scale for overall, emotional, and social loneliness: Confirmatory tests on survey data. *Research on Aging*, 28(5), 582–598. 10.1177/0164027506289723
- Greene M, Hessel NA, Perissinotto C, Zepf R, Hutton Parrott A, Foreman C, Whirry R, Gandhi M, & John M (2018). Loneliness in older adults living with HIV. *AIDS and Behavior*, 22(5), 1475–1484. 10.1007/s10461-017-1985-1 [PubMed: 29151199]
- Hackett RA, Hamer M, Endrighi R, Brydon L, & Steptoe A (2012). Loneliness and stress-related inflammatory and neuroendocrine responses in older men and women. *Psychoneuroendocrinology*, 37(11), 1801–1809. 10.1016/j.psyneuen.2012.03.016 [PubMed: 22503139]
- Han SD, Adeyemi O, Wilson RS, Leurgans S, Jimenez A, Oullet L, Shah R, Landay A, Bennett DA, & Barnes LL (2017). Loneliness in older Black adults with human immunodeficiency virus is associated with poorer cognition. *Gerontology*, 63(3), 253–262. 10.1159/000455253 [PubMed: 28125811]
- Harris M, Brouillette M-J, Scott SC, Smail F, Smith G, Thomas R, Fellows LK, & Mayo NE (2020). Impact of loneliness on brain health and quality of life among adults living with HIV in Canada. *Journal of Acquired Immune Deficiency Syndromes*, 84(4), 336–344. 10.1097/qai.0000000000002355 [PubMed: 32598116]

- Hawkley LC, & Cacioppo JT (2010). Loneliness matters: A theoretical and empirical review of consequences and mechanisms. *Annals of Behavioral Medicine*, 40(2), 218–227. 10.1007/s12160-010-9210-8 [PubMed: 20652462]
- Hawkley LC, Cole SW, Capitanio JP, Norman GJ, & Cacioppo JT (2012). Effects of social isolation on glucocorticoid regulation in social mammals. *Hormones and Behavior*, 62(3), 314–323. 10.1016/j.yhbeh.2012.05.011 [PubMed: 22663934]
- Hong S, & Banks WA (2015). Role of the immune system in HIV-associated neuroinflammation and neurocognitive implications. *Brain, Behavior, and Immunity*, 45, 1–12. 10.1016/j.bbi.2014.10.008 [PubMed: 25449672]
- Hosaka KRJ, Greene M, Premeaux TA, Javandel S, Allen IE, Ndhlovu LC, & Valcour V (2019). Geriatric syndromes in older adults living with HIV and cognitive impairment. *Journal of American Geriatrics Society*, 67(9), 1913–1916. 10.1111/jgs.16034
- Hyland P, Shevlin M, Cloitre M, Karatzias T, Vallières F, McGinty G, Fox R, & Power JM (2019). Quality not quantity: Loneliness subtypes, psychological trauma, and mental health in the US adult population. *Social Psychiatry and Psychiatric Epidemiology*, 54(9), 1089–1099. 10.1007/s00127-018-1597-8 [PubMed: 30293176]
- Käll A, Shafran R, Lindegaard T, Bennett S, Cooper Z, Coughtrey A, & Andersson G (2020). A common elements approach to the development of a modular cognitive behavioral theory for chronic loneliness. *Journal of Consulting and Clinical Psychology*, 88(3), 269–282. 10.1037/ccp0000454 [PubMed: 32068427]
- Kroenke K, Wu J, Yu Z, Bair MJ, Kean J, Stump T, & Monahan PO (2016). Patient health questionnaire anxiety and depression scale: Initial validation in three clinical trials. *Psychosomatic Medicine*, 78(6), 716–727. 10.1097/PSY.0000000000000322 [PubMed: 27187854]
- Lam JA, Murray ER, Yu KE, Ramsey M, Nguyen TT, Mishra J, Martis B, Thomas ML, & Lee EE (2021). Neurobiology of loneliness: A systematic review. *Neuropsychopharmacology*, 46(11), 1873–1887. 10.1038/s41386-021-01058-7 [PubMed: 34230607]
- Lee JH, Luchetti M, Aschwanden D, Sesker AA, Strickhouser JE, Terracciano A, & Sutin AR (2022). Cognitive impairment and the trajectory of loneliness in older adulthood: Evidence from the health and retirement study. *Journal of Aging and Health*, 34(1), 3–13. 10.1177/08982643211019500 [PubMed: 34027689]
- Manoli A, McCarthy J, & Ramsey R (2022). Estimating the prevalence of social and emotional loneliness across the adult lifespan. *Scientific Reports*, 12(1), 21045. 10.1038/s41598-022-24084-x [PubMed: 36473900]
- Miller EN, Satz P, & Visscher B (1991). Computerized and conventional neuropsychological assessment of HIV-1-infected homosexual men. *Neurology*, 41(10), 1608–1616. 10.1212/wnl.41.10.1608 [PubMed: 1922803]
- O'Súilleabháin PS, Gallagher S, & Steptoe A (2019). Loneliness, living alone, and all-cause mortality: The role of emotional and social loneliness in the elderly during 19 years of follow-up. *Psychosomatic Medicine*, 81(6), 521–526. 10.1097/psy.0000000000000710 [PubMed: 31094903]
- Patton JH, Stanford MS, & Barratt ES (1995). Factor structure of the Barratt impulsiveness scale. *Journal of Clinical Psychology*, 51(6), 768–774. 10.1002/1097-4679(199511)51:6<768::aid-jclp2270510607>3.0.co;2-1 [PubMed: 8778124]
- Penning MJ, Liu G, & Chou PHB (2014). Measuring loneliness among middle-aged and older adults: The UCLA and De Jong Gierveld loneliness scales. *Social Indicators Research*, 118(3), 1147–1166. 10.1007/s11205-013-0461-1
- Rast P, Zimprich D, Van Boxtel M, & Jolles J (2009). Factor structure and measurement invariance of the cognitive failures questionnaire across the adult life span. *Assessment*, 16(2), 145–158. 10.1177/1073191108324440 [PubMed: 19066391]
- Reitan R, & Wolfson D (1985). *The Halstead-Reitan Neuropsychological Test Battery: Theory and clinical interpretation*. Neuropsychology Press.
- Rey A (1941). L'examen psychologique dans les cas d'encephalopathie traumatique. (Les problems). *Archives de Psychologie*, 28, 215–285. <https://psycnet.apa.org/record/1943-03814-001>
- Roth RM, Isquith PK, & Gioia GA (2005). Behavior Rating Inventory of Executive Function®—Adult Version (BRIEF-A). Psychological Assessment Resources Lutz, FL. 10.1037/t86244-000

- Rubin LH, Xu Y, Norris PJ, Wang X, Dastgheyb R, Fitzgerald KC, Keating SM, Kaplan RC, Maki PM, Anastos K, Springer G, Benning L, Kassaye S, Gustafson DR, Valcour VG, & Williams DW (2020). Early inflammatory signatures predict subsequent cognition in long-term virally suppressed women with HIV. *Frontiers in Integrative Neuroscience*, 14, 20. 10.3389/fnint.2020.00020 [PubMed: 32390808]
- Salinas J, Beiser AS, Samra JK, O'Donnell A, DeCarli CS, Gonzales MM, Aparicio HJ, & Seshadri S (2022). Association of loneliness with 10-year dementia risk and early markers of vulnerability for neurocognitive decline. *Neurology*, 98(13), e1337–e1348. 10.1212/wnl.000000000200039 [PubMed: 35131906]
- Schretlen DJ, Winicki JM, Meyer SM, Testa SM, Pearlson GD, & Gordon B (2009). Development, psychometric properties, and validity of the Hopkins Adult Reading Test (HART). *The Clinical Neuropsychologist*, 23(6), 926–943. 10.1080/13854040802603684 [PubMed: 19191072]
- Smit M, Brinkman K, Geerlings S, Smit C, Thyagarajan K, Sighem A. v., de Wolf F, Hallett TB, & ATHENA observational cohort (2015). Future challenges for clinical care of an ageing population infected with HIV: A modelling study. *The Lancet Infectious Diseases*, 15(7), 810–818. 10.1016/S1473-3099(15)00056-0 [PubMed: 26070969]
- Sundström A, Adolfsson AN, Nordin M, & Adolfsson R (2020). Loneliness increases the risk of all-cause dementia and Alzheimer's disease. *The Journals of Gerontology Series B, Psychological Sciences and Social Sciences*, 75(5), 919–926. 10.1093/geronb/gbz139 [PubMed: 31676909]
- Sutin AR, Stephan Y, Luchetti M, & Terracciano A (2020). Loneliness and risk of dementia. *The Journals of Gerontology Series B, Psychological Sciences and Social Sciences*, 75(7), 1414–1422. 10.1093/geronb/gby112 [PubMed: 30365023]
- Valcour V, Sithinamsuwan P, Letendre S, & Ances B (2011). Pathogenesis of HIV in the central nervous system. *Current HIV/AIDS Reports*, 8(1), 54–61. 10.1007/s11904-010-0070-4 [PubMed: 21191673]
- Wechsler D (1981). Wechsler Adult Intelligence Scale—Revised. Psychological Corporation.
- Weiss R (1975). Loneliness: The experience of emotional and social isolation. MIT Press.
- Wolters NE, Mobach L, Wuthrich VM, Vonk P, Van der Heijde CM, Wiers RW, Rapee RM, & Klein AM (2023). Emotional and social loneliness and their unique links with social isolation, depression and anxiety. *Journal of Affective Disorders*, 329, 207–217. 10.1016/j.jad.2023.02.096 [PubMed: 36842647]
- Yoo-Jeong M, Hepburn K, Holstad M, Haardörfer R, & Waldrop-Valverde D (2020). Correlates of loneliness in older persons living with HIV. *AIDS Care*, 32(7), 869–876. 10.1080/09540121.2019.1659919 [PubMed: 31462066]

Key Considerations

- Emotional loneliness is related to processing speed and executive function above and beyond the influence of depressive symptoms.
- As loneliness is modifiable, interventions aimed at reducing emotional loneliness may be helpful in improving specific cognitive domains.
- Intervention efforts targeting emotional loneliness, such as, ways to address social cognition and improving perception to intimate social relationships, would help older people with HIV to strengthen cognitive function.

Table 1.

Sample Characteristics

		<i>n</i> (%)	
Male		20 (48)	
Race			
White		9 (21)	
Black		31 (74)	
Other		2 (5)	
Ethnicity			
Hispanic		2 (5)	
Non-Hispanic		40 (95)	
HIV RNA viral load			
< 20cp/ml (viral suppression)		39 (93)	
> 20 and < 100 cp/ml		3 (7)	
	<i>M</i> (SD)	Minimum	Maximum
Age	61.5 (6.7)	50	76
Years of education	13.3 (2.6)	8	20
Hopkins Adult Reading Test	16.6 (7.8)	4	33
			Median (IQR)
PHQ-9 [†]		3.2 (4.3)	
None-minimal (0–4)		31 (74)	
Mild (5–9)		7 (17)	
Moderate (10–14)		3 (7)	
Moderately severe (15–19)		0 (0)	
Severe (> 20)		1 (2)	
CD4+ T cell count		686.8 (331.4)	
	Objective cognition	<i>M</i> (SD)	Minimum
HVLt-R			
Total learning (outcome = total correct)		23.3 (5.9)	9
Delay free recall (outcome = total correct)		8.1 (2.5)	3
Recognition (outcome = hits – false positives)		9.7 (2.1)	1
ROCF (outcome = total correct)			
Immediate free recall		15.0 (6.9)	4.5
Delay free recall		15.3 (7.0)	5
Letter fluency (outcome = total correct)		27.6 (11.0)	11
Animal fluency (outcome = total correct)		18.0 (4.8)	8
Digit Symbol (outcome = total correct)		44.4 (12.7)	18
GPEG (outcome=time to completion) [‡]			
Dominant hand		90.5 (27.6)	58
			194

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

			<i>n</i> (%)
Non-dominant hand	107.2 (71.1)	59	526
TMT (outcome = time to completion) [†]			
Part A	33.1 (13.2)	16	76
Part B	94.7 (66.9)	26	311
Stroop (outcome = time to completion) [†]			
Color trial	59.8 (20.4)	37	127
Interference trial	129.9 (43.1)	58	257
CalCAP (outcome = median reaction time) [†]			
Choice	461.5 (66.7)	365	663
Sequential	606.4 (152.0)	385	856
Subjective cognition[†]	<i>M</i> (SD)	Minimum	Maximum
CFQ total score (range: 0–100)	32.7 (15.5)	0	70
BRIEF—adult version subscales			
Inhibition (range: 8–24)	11.5 (2.9)	8	18
Monitor (range: 6–18)	8.9 (2.4)	6	14
Set-shift (range: 6–18)	9.0 (2.6)	6	15
Working memory (range: 8–24)	12.5 (4.0)	8	21
Planning and organization (range: 10–30)	14.8 (4.7)	10	25
BIS (range: 30–120)	57.3 (9.4)	39	74

Note: *N* = 42. BIS= Barrett Impulsiveness Scale; BRIEF = Behavior Rating Inventory of Executive Function; CalCAP= California Computerized Assessment Package; CFQ = Cognitive Failures Questionnaire; GPEG = Grooved PegboardTM; HVLT-R = Hopkins Verbal Learning Test-Revised; IQR = interquartile range; OPWH = older persons with HIV; PHQ-9 = Patient Health Questionnaire; ROCF = Rey-Osterrieth Complex Figure Test; TMT = Trail Making Test;

[†] higher scores = poorer performance or more symptoms; the range provides the range of possible scores on the scale/subscales.

Table 2.

Sociodemographic Covariates Adjusted Hierarchical Multivariable Regression on Loneliness and Cognition

	Overall loneliness			Loneliness subtypes		
	Model 1	Model 2		Model 2		
Cognitive outcomes	R ²	R ²	β	R ²	Emotional β	Social β
Objective						
Letter fluency	0.40 ^{***}	0.10 [*]	-0.34 [*]	0.10 [*]	-0.26 [*]	-0.20
Digit symbol	0.46 ^{***}	0.06 [*]	-0.26 [*]	0.15 ^{**}	-0.41 ^{***}	0.09
GPEG: non-dominant	0.25 [*]	0.10 [*]	-0.34 [*]	0.11 [†]	-0.27 [†]	-0.16
TMT: Part A	0.36 ^{**}	0.09 [*]	-0.32 [*]	0.10 [*]	-0.30 [*]	-0.11
TMT: Part B	0.22 [*]	0.08 ^T	-0.30 ^T	0.11 [‡]	-0.32 [*]	-0.06
Stroop: Trial 3-interference	0.38 ^{**}	0.03	-0.19	0.06	-0.26 [*]	0.02
CalCAP: sequential — simple	0.12	0.10 [*]	-0.33 [*]	0.14 [*]	-0.38 [*]	-0.04
Subjective						
CFQ	0.02	0.13 [*]	0.38 [*]	0.13	0.27	0.22 [‡]
BIS	0.19	0.16 ^{**}	0.42 ^{**}	0.16 [*]	0.26 [‡]	0.29 [†]
BRIEF						
Inhibit	0.15	0.21 ^{**}	0.49 ^{**}	0.21 ^{**}	0.28 [*]	0.36 [*]
Shift	0.19	0.25 ^{***}	0.54 ^{***}	0.25 ^{**}	0.38 ^{**}	0.31 [*]
Self-monitor	0.19	0.16 ^{**}	0.42 ^{**}	0.16 [*]	0.23	0.32 [*]
Working memory	0.18	0.20 ^{**}	0.48 ^{**}	0.21 ^{**}	0.37 [*]	0.25
Plan/organize	0.22 ^T	0.19 ^{**}	0.47 ^{**}	0.19 ^{**}	0.30 [*]	0.30 [*]

Note. N = 42.

*** p < .001;

** p < .01;

* p < .05;

^T p = 0.05;

[†] p = 0.06;

[‡] p = 0.07 for change statistics and standardized beta coefficients (β); Model 1 includes age, sex, race, and education; Model 2 includes Model 1 variables and loneliness (separately for overall loneliness and loneliness subscales); Negative β's for objective cognitive measures (CalCAP [California Computerized Assessment Package]; Grooved PegboardTM [GPEG]; Trail Making Test [TMT]) indicates more cognitive problems; Positive β's for self-reported cognitive questionnaires (Cognitive Failures Questionnaire [CFQ]; Behavior Rating Inventory of Executive Function [BRIEF]; Barrett Impulsiveness Scale [BIS]) indicate more cognitive complaints.

Table 3.

PHQ-9 Adjusted Hierarchical Multivariable Regression on Loneliness and Cognition

	PHQ-9			Overall loneliness		Loneliness subtypes		
	Model 1	Model 2		Model 3		Model 3		
Cognitive outcomes	R ²	R ²	β	R ²	β	R ²	Emotional β	Social β
Objective								
Letter fluency	0.40 ^{***}	0.03	-0.18	0.07 [*]	-0.33 [*]	0.07	-0.25 [‡]	-0.17
Digit symbol	0.46 ^{***}	0.07 [*]	-0.27 [*]	0.01	-0.14	0.10 [*]	-0.34 ^{**}	0.13
GPEG: non-dominant	0.25 [*]	0.01	-0.10	0.10 [*]	-0.39 [*]	0.10 [‡]	-0.32 ^T	-0.19
TMT: Part A	0.36 ^{**}	0.08 [*]	-0.29 [*]	0.03	-0.22	0.04	-0.23	-0.06
TMT: Part B	0.22 [*]	0.05	-0.23	0.03	-0.23	0.06	-0.28	-0.17
Stroop: Trial 3-interference	0.38 ^{**}	0.01	-0.10	0.02	-0.19	0.06	-0.27 [‡]	0.01
CalCAP: sequential — simple	0.12	0.03	-0.17	0.07	-0.33	0.12	-0.39 [*]	-0.04
Subjective								
CFQ	0.02	0.25 ^{**}	.50 ^{**}	0.01	0.14	0.01	0.09	0.09
BIS	0.19	0.11 [*]	0.33 [*]	0.07 [‡]	.33 ^T	0.07	0.18	0.24
BRIEF								
Inhibit	0.15	0.18 ^{**}	.43 ^{**}	0.07 [*]	.34 [*]	0.08	0.16	0.28 [‡]
Shift	0.19	0.23 ^{***}	.48 ^{***}	0.08 [*]	.36 [*]	0.08	0.25	0.22
Self-monitor	0.19	0.21 ^{**}	.46 ^{***}	0.03	0.23	0.04	0.08	0.22
Working memory	0.18	0.35 ^{***}	.60 ^{***}	0.02	0.20	0.03	0.16	0.11
Plan/organize	0.22 ^T	0.31 ^{***}	.56 ^{***}	0.03	0.21	0.03	0.10	0.17

Note. *N* = 42.

^{***} *p* < .001;

^{**} *p* < .01;

^{*} *p* < .05;

^T *p* = .05;

[‡] *p* = .06;

[‡] *p* = .07 for change statistics and standardized beta coefficients (β); Model 1 includes age, sex, race, and education; Model 2 includes Model 1 variables and depressive symptoms (Patient Health Questionnaire [PHQ-9] total score); Model 3 includes Model 1 and 2 variables and loneliness (separately for overall loneliness and loneliness subscales); Negative β's for objective cognitive measures (CalCAP [California Computerized Assessment Package]; Grooved PegboardTM [GPEG]; Trail Making Test [TMT]) indicates more cognitive problems; Positive β's for self-reported cognitive questionnaires (Cognitive Failures Questionnaire [CFQ]; Behavior Rating Inventory of Executive Function [BRIEF]; Barrett Impulsiveness Scale [BIS]) indicate more cognitive complaints.