Rehabilitation of HIV-associated neurocognitive disorder: a systematic scoping review of available interventions

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Abstract

Objective: Strong healthcare systems require rich rehabilitation protocols for improving the outcomes of disabling ailments such as HIV-associated neurocognitive disorder (HAND). Currently, the rehabilitative interventions for HAND are unknown. We thus reviewed the putative rehabilitative interventions for HAND and evaluated their post-treatment outcomes.

Methods: This is a systematic scoping review of articles published in English, between 2009 and 2019. The review was guided by the PRISMA extension for scoping reviews. We searched for articles in PubMed, MEDLINE, Cochrane Library, CINAHL, Academic Search Complete and PsycINFO. Data were selected and extracted according to predesigned eligibility criteria using a standardised data extraction table. We appraised the methodological quality of the included studies using the Mixed Method Appraisal Tool.

Results: We identified 423 records, which were screened for eligibility. Twenty two articles were identified, representing a sample of 2795 PLWHIV, who were on average 47 ± 8 years old, with 13 ± 3 years of education. From the reviewed literature, we identified two putative rehabilitative intervention options for HAND, namely cognitive training otherwise known as psycho-cognitive training, and physical activity interventions. All articles reporting on cognitive training for HAND showed improved post-treatment performance, while two of the six interventional physical activity studies recorded improved post-treatment cognitive performance.

Discussion: There are limited rehabilitative options available for HAND. Psycho-cognitive training appears to be an effective intervention for HAND, however, the conditions of far-transfer effects need to be set forth. There is insufficient evidence available to support the use of physical activity for HAND thus warranting further research.

Registration: The review protocol was registered with Open Science Framework (OSF) registry. The registration DOI:10.17605/OSF.IO/RWQCF.

KEYWORDS: HIV; neurocognitive disorder; rehabilitation; intervention; scoping review

Introduction

Despite the growing need to treat mental health challenges among people living human immunodeficiency virus (PLWHIV) worldwide, the present HIV care system does not adequately integrate rehabilitative measures in management of HIV-associated neurocognitive disorder (HAND) (Chetty, Maddocks, Cobbing, & Hanass-Hancock, 2018). HAND is a common neurological condition among PLWHIV which limits social participation and impairs well-being (Hawkins, Brown, Margolick, & Erlandson, 2017; Yakasai et al., 2015). Globally, HAND affects 50% of PLWHIV, although rates vary across countries (Clifford, 2017), negatively impacting quality of life (QoL) and treatment adherence (Morgan, Woods, & Grant, 2012). It is typified by behavioural and motor abnormalities such as memory loss, impulsiveness, irritability, visuospatial difficulty, difficulty with mathematical tasks, concentration and attention (Clifford & Ances, 2013; Modi, Mochan, & Modi, 2018). These abnormalities may severely impair ability to perform daily activities resulting in low productivity, loss of employment, poverty and poor QoL (Alford & Vera, 2018).

Managing HIV and HIV-related neurological complications has received appreciable global response and represents one of the public health advancements of the century (Alkali, Bwala, Nyandaiti, & Danesi, 2013). Notwithstanding, HIV remains a public health issue especially in resource constrained sub-Saharan Africa where more than half of PLWHIV live (Nweke, Mshunqane, Govender, & Akinpelu, 2021). Antiretroviral therapy (ART) and the early intensification approach have undoubtedly improved QoL and longevity, making HIV a chronic disease (Deeks, Lewin, & Havlir, 2013). The chronic nature of HIV has resulted in a higher prevalence of neurological and neuropsychological complications in the ART era. In particular, HAND is more common among the ageing population of PLWHIV, who seem to age faster and are predisposed to frailty (Guaraldi et al., 2011). HAND could be the result of the primary HIV infection, long term burden of ART or ART related neurotoxicity (Kumar et al., 2019; Thakur et al., 2019). Interestingly, universal healthcare coverage for PLWHIV in southern Africa is projected to reduce HIV-related mortality, while increasing the number of PLWHIV in need of chronic rehabilitative care (Chetty et al., 2018). In the next decade, more PLWHIV will be thus be diagnosed with HAND and similar complications of chronic HIV. The continuous use of ART to treat HAND has been reported, but may be limited by drug resistance, virologic failure, adverse drug events, neurotoxicity, renal failure and poor access to ART, among other factors (Thakur et al., 2019; Weber, Blackstone, & Woods, 2013). As with any chronic care system, there is a need for an inclusive HIV care system with rehabilitation arm, when reintegrating HIV survivors back into society (Society of Neuroscientists of Africa, 2015).

Interestingly, cognitive challenges in HIV seronegative patients have proved to respond to some neurorehabilitative interventions (Becker et al., 2012; Vance, Fazeli, Ross, Wadley, & Ball, 2012). Unfortunately, the treatment of HAND and the reintegration of PLWHIV into communities has received little attention (O'Brien et al., 2014). This weakness may be blamed on unsuspecting HIV policies and planning, limited financial and manpower resources as well as lack of adequate skill among HIV care professionals to diagnose and treat HAND (Banks, Zuurmond, Ferrand, & Kuper, 2017; Devendra, Makawa, Kazembe, Calles, & Kuper, 2013). Strengthening healthcare systems with putative rehabilitation intervention options is pivotal in the fight against chronic HIV and related mental health challenges. In light of the limited options available for rehabilitative interventions for people living with HAND, this study aimed to conduct a systematic scoping review to map out evidence on rehabilitative intervention options for HAND.

Objectives: The objectives were to identify the available rehabilitation intervention options for HAND and to evaluate the post-treatment outcomes following specific interventions.

Methods

The literature review was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) (Tricco et al., 2018).

Protocol and registration

The study protocol was registered with the Open Sciences Frame (OSF) review registry on the 9th December 2019. The protocol is accessible at osf.io/jb2xf. The registration DOI:10.17605/OSF.IO/RWQCF.

Eligibility criteria

Inclusion criteria

- Only studies reporting evidence on putative rehabilitation interventions for HAND
- Only studies conducted among adult PLWHIV
- Articles written and published in English
- Only studies published between 2009 and 2019

Exclusion criteria

- Opinion papers on rehabilitation interventions for HAND
- Commentaries on rehabilitation interventions for HAND
- Studies on rehabilitation interventions for children living with HAND
- *All studies not published in English*

Information source

At the protocol stage, we proposed searching eight databases. We dropped SportDiscuss because it yielded no relevant articles during the initial search. The remaining search engines included PubMed, Cochrane Library, MEDLINE, CINAHL, Academic Search Complete, and PsycINFO. We also searched the reference lists of relevant articles for additional studies.

Search

We employed keywords and MeSH terms from key articles. We then analysed the keywords and index terms used to describe the articles. We conducted a pilot search using these terms in PubMed. We refined the search terms to obtain the most sensitive and specific strategy (see Appendix A). A third search using the piloted terms was conducted across all selected databases.

Screening and selection process

All search results were exported into EndNote X8, and duplicate studies removed. We screened the article titles and abstracts using pre-defined eligibility criteria. Next, we analysed the full texts of the selected studies. Details of the selection process are presented in Figure 1.

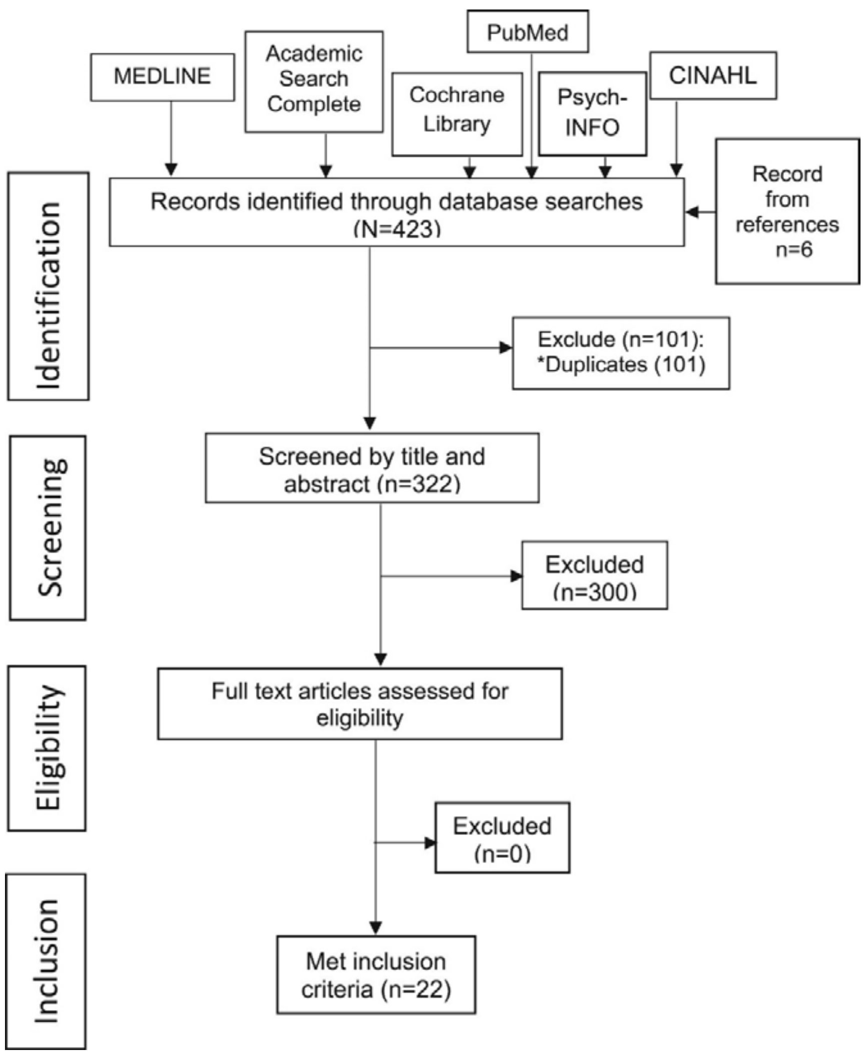

Figure 1. PRISMA-ScR flow diagram showing the process used to select articles describing rehabilitation interventions for people suffering from HIV-associated neurocognitive disorder (HAND).

Charting the data

We used a valid data charting tool from the Joanna Briggs Institute (2015) to extract and capture information from studies through each phase of the review. The chart was continuous and updated regularly. The following key information is presented in the evidence pooled table (Table 1): authors, year of publication, sample size, study design, intervention, comparator, outcome measure, study quality and key findings.

Data items

We searched for articles focussing on rehabilitation interventions and cognitive function in PLWHIV. According to the World Health Organisation (2019), rehabilitation interventions are needed when a person is experiencing limited everyday functioning due to ageing or health conditions, including chronic diseases or disorders, injuries or traumas. Examples of rehabilitation interventions include physical exercise, acupuncture, mental imagery and neuropsychological interventions. According to the U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion (2010), HAND is a range of increasingly severe central nervous system complications associated with HIV infection, which require rehabilitation.

Critical appraisal

In line with the recommendation of Levac, Colquhoun, and O'Brien (2010), we assessed the quality of the included studies. Consumers of health information should exercise caution when choosing a rehabilitation intervention for any condition, including HAND. We critically assessed the selected studies using the mixed method appraisal tool (MMAT) Version 2011 (Hong et al., 2018). The MMAT examines the appropriateness of the aim of the study, adequacy and methodology, study design, participant recruitment, data collection, data analysis, presentation of findings, authors' discussions and conclusions.

Ethical consideration

This review was approved by the Research Ethics Committee of the Faculty of Health Sciences, University of Pretoria (Ethics Reference Number: 152/2020), which complies with the ICH-GCP guidelines.

Synthesis of results

In the protocol, we had planned to employ NVIVO aided thematic analysis but later decided to use quantitative synthesis because we needed to evaluated their post-treatment outcomes. We provided a narrative account of the extracted data, supported by a quantitative analysis. Data are presented in evidence pooled Tables 1–3. We extracted themes including 'rehabilitative interventions options for HAND, post-treatment outcome/result and cognitive assessment and tools'. Finally, putative rehabilitative interventions for HAND were mapped.

Results

Review profile

We identified a total of 423 articles, of which 101 duplicates were removed. The remaining 322 publications were screened for eligibility, of which 22 met the inclusion criteria (Figure 1). The included studies were published between 2012 and 2019, with an overall sample size of 2795 people. The studies comprised 14 interventional and 8 observational studies. Fifteen (68%) of the included studies focused on physical activity (7 interventional and 8 observational studies), while 7 (6 interventional and 1 systematic review) focused on cognitive exercise. Sixteen (73%) studies were conducted in United States of America (USA). Of the included studies, nine were RCTs, five case–control, four cohort, and four cross-sectional studies.

Sociodemographic characteristics of the study participants and quality appraisal

All the studies included a total of 2795 PLWHIV with a mean age of 47 ± 8 years and 13 ± 3 years of education. For interventional studies, the sample size varied from 11 to 99 participants, and from 3 to 988 for non-interventional studies. Sixty percent of the all participants were men and 54% were white (Table 2). Approximately 19% of participants participated in interventional studies. We undertook quality appraisal with the aid of the MMAT. Result revealed that 5/6 of the cognitive studies were pilot studies hence samples were not representative of the target population. Similarly, in 2/6 of the interventional PA studies, samples were not representive of the target population, with cognitive impairment was measured using the MOS-HIV-cognitive subscale instead of gold standard comprehensive neuropsychological testing. Most (5/6) of the observational PA studies utilised non-probability sampling strategy (Tables 2 and 3).

Neurocognitive assessment and tools

To measure cognitive function, 14 (64%) articles used neuropsychological battery tests covering 3–11 domains, two articles used the MOS-HIV-cognitive subscale, two articles used the FAHI scale and one study used the Montreal cognitive assessment scale. For neuropsychological testing, three studies (two on cognitive exercise and one observational physical activity study) (Casaletto et al., 2016; Chow et al., 2019; Vance et al., 2012) did not cover the minimum five cognitive domains which, in line with Frascati criteria, are a requirement for the diagnosis of HAND (Anitori et al., 2007). More than half of the studies used more than one neuropsychological test to measure most cognitive domains. The most commonly used test for reasoning or information processing speed was TMT-A, followed by the Stroop Colour and Word Test. Attention and concentration was most commonly measured using the Wechsler Adult Intelligence Scale-III (WAIS-III) Digit Span Subtest. Executive function was most commonly measured using the Trail Making Test B, followed by the Wisconsin Card Sorting Test. Verbal fluency and language was most frequently measured using the Verbal Fluency (FAS), followed by Category Fluency (animals). Learning and recall was most commonly measured using the Hopkins Verbal Learning Test-Revised. Working memory was most frequently evaluated using the Paced Auditory Serial

Table 1. Evidence table displaying putative rehabilitation intervention options for cognitive impairment among PLWHIV.

Author (s)	Title	Country, design & sample size	Intervention/exposure	Outcome & outcome measure(s)	Summary of findings
PA studies					
Baigis et al. (2002)	Effectiveness of a home-based exercise intervention for HIV-infected adults: a randomised trial	-USA -RCT -99	15 wk of 20-min aerobic exercise 3/wk for (75–85%) HR peak (total dose = 15 h) vs. control (no exercise)	Medical Outcomes Study (MOS)-HIV-cognitive subscale	no change in cognitive subscale scores ($P = 0.86$)
Fillipas et al. (2006)	A six-month, supervised, aerobic and resistance exercise program improves self-efficacy in people with human immunodeficiency virus: a randomised controlled trial	-Australia -RCT -40	6months of 1-h aerobic (60–75% HRmax) and resistance exercise (60–80% 1RM) 2/week (total dose = 52 h) vs. control (20-min walking sessions 2/wk)	MOS-HIV-cognitive subscale	exercise group improved 14 points compared to control ($p = 0.04$)
Galantino et al. (2005)	The effect of group aerobic exercise and T'ai chi on functional outcomes and quality of life for persons living with acquired immunodeficiency syndrome	-USA -RCT -38	8 wk of 1-h class twice/wk of Tai Chi vs strength and endurance (<60–70% HR reserve) exercise (total dose = 16 h) vs control (no exercise)	MOS-HIV-cognitive subscale	No significant group differences ($p = 0.46$)
Brown et al. (2016)	Evaluation of a physiotherapy-led group rehabilitation intervention for adults living with HIV: referrals, adherence and outcomes	-UK -Cohort design -92	10 wk of 1-h moderate to vigorous exercise (aerobic, neuromotor, resistive:70% 1RM, 1–3 sets,8–15 reps) 2/wk (total dose = 20 h)	Functional Assessment of HIV Infection (FAHI)-cognitive subscale	no change in cognitive subscale scores ($p = 0.635$)
Schlabe et al. (2017)	Moderate endurance training (marathon-training) – effects on immunologic and metabolic parameters in HIV-infected patients: the 42 KM cologne project.	-Germany -Cohort design -21	Progressive aerobic training, 3–10 h/week (3–4 weekly sessions) at 60–80% of HRmax, and sprints for 12 months vs. HIV preference group, gathered longitudinal data on interventional group only	MOS-HIV-cognitive subscale	No change in MOS-HIV cognitive subscale scores ($p > 0.05$)
McDermott et al. (2017)	The effects of a 16-week aerobic exercise programme on cognitive function in people living with HIV	-Ireland -RCT -11	Structure physical activity-aerobic exercise. Three times per week for twelve weeks.	Montreal cognitive assessment & seven-day accelerometery	No significant improvements in cognitive function or aerobic fitness ($P > 0.05$).
Robins et al. (2006)	Research on psychoneuroimmunology: Tai Chi as a stress management approach for individuals with HIV disease	-USA -Cohort design -59	10 wk of 1-h Tai Chi once/wk (total dose = 10 h)	FAHI-cognitive subscale	FAHI: significant pre–post change ($p = 0.042$) in cognitive subscale
Dufour et al. (2013)	Physical exercise is associated with less neurocognitive impairment among HIV-infected adults	-USA -Case control -335	Unstructured physical activity	Neuropsychological battery testing 7 cognitive domains & staff-administered physical activity questionnaire	HIV infected adults who exercised were approximately half as likely to show NCI as compared to those who had no exercise ($P < 0.05$; OR = 2.19; CI = 1.03–4.68)
Dufour et al. (2018)	A longitudinal analysis of the impact of physical activity on neurocognitive functioning among HIV-Infected adults	-USA Prospective cohort -235	Unstructured physical activity	Neuropsychological battery testing 7 cognitive domains & staff-administered physical activity questionnaire	PA group began with, and maintained, significantly better neurocognitive function compared to the those who with either inconsistent PA or nil PA (OR = 1.28; SE = 0.33; $p = 0.001$)
Fazeli et al. (2014)	Active lifestyle is associated with better neurocognitive functioning in adults living with HIV infection	-USA -Cross-sectional survey -139	Unstructured physical activity	Neuropsychological battery testing 7 cognitive domains & staff-administered physical activity questionnaire	Increased active lifestyle was associated with better global neurocognitive performance as well as a lower prevalence of HAND (OR = 0.59; CI = 0.36–0.93; $P = 0.02$).

Fazeli et al. (2015)	Physical activity is associated with better neurocognitive and everyday functioning among older adults with HIV disease	-USA -Cross-sectional survey -100	Unstructured physical activity	Neurocognitive battery testing 7 cognitive domains & international physical activity questionnaire (IPAQ)	Higher levels of moderate PA were associated with lower odds of NCI (OR = 0.94; $p = 0.01$), even when covariates were modelled.
Mapstone et al. (2013)	Poor aerobic fitness may contribute to cognitive decline in HIV-infected older adults	-USA -Case control -37	Unstructured physical activity	Neuropsychological battery testing 6 cognitive domains & aerobic fitness-(VO_2max) – progressive treadmill test	Participants with higher VO2peak were less likely to have more severe forms of HAND – i.e. MNC (OR=0.65; $p = 0.01$) and HAD (OR = 0.64; $p =$ 0.0006)
Monroe et al. (2017)	The association between physical activity and cognition in men with and without HIV infection	-USA -Case control -601	Unstructured physical activity	Neuropsychological battery testing 5 cognitive domains & IPAQ	High PA was associated with lower odds of impairment of learning, memory, and motor function odds ratio (OR) ranging from 0.52–0.57; $P < 0.05$ for all.
Chow et al. (2019)	Physical activity is associated with lower odds of cognitive impairment in women but not men living with human immunodeficiency virus infection	-USA -Cross-sectional -988	Unstructured physical activity	Brief Neuropsychological battery testing 3 domains	In a multivariable model, physical activity was associated with lower odds of cognitive impairment in women (odds ratio, 0.35; CI = 0.15–0.80; $P =$ 0.013) but not men
Ortega et al. (2015)	Physical activity affects brain integrity in HIV + individuals	-USA -Cross-sectional survey -70	Unstructured physical activity	Neuropsychological battery testing 7 cognitive domains & a self-reported exercise questionnaire	Physically active HIV + individuals performed better on executive ($p = .040$, unadjusted; $p = .043$, adjusted) but not motor function ($p = .17$)
CE studies					
Vance et al. (2019)	Computerised cognitive training for the neurocognitive complications of HIV infection: A systematic review	USA	Cognitive exercise/training	-Not applicable	Cognitive training improves cognitive function. One case study even demonstrated a reversal of HIV-associated neurocognitive disorder after cognitive training.
Bai et al. (2018)	Efficacy of a computerised cognitive rehabilitation training in improving HIV-associated neurocognitive disorders	-Italy -RCT -28	Nine sessions of computer-based cognitive exercises	Neuropsychological battery testing 7 cognitive domains	At the 12th week, the proportion of HAND has declined with no cognitive impairment in 2/7 (28%) patients. The mean T scores in two cognitive domains namely attention/working memory and abstraction/executive ($P = 0.04$)
Towe et al. (2017)	The acceptability and potential utility of cognitive training to improve working memory in persons living with HIV: A preliminary randomised trial	-USA -Placebo-RCT -21	12 training sessions across 10 weeks	Neuropsychological battery testing 7 cognitive domain	Participants in the experimental arm demonstrated improved working memory function over time ($P < 0.05$); participants in the control arm showed no change ($P > 0.05$).
Vance et al. (2012)	Speed of processing training with middle-age and older adults with HIV: A pilot study	-USA -RCT -46	Cognitive exercise/ Training – speed of processing (SOP)	Brief neuropsychological battery testing 3 domains	Specifically, participants in the speed of processing training group experienced improved speed of processing ($P = 0.04$) and improved everyday functioning ($P = 0.03$)
Livelli et al. (2015)	Evaluation of a cognitive rehabilitation protocol in HIV patients with associated neurocognitive disorders: Efficacy and stability over time	-Italy -RCT -32	Cognitive exercise training 10 1-hr sessions of cognitive exercise over 5-6weeks period	Neuropsychological battery testing 7 cognitive domains	The experimental group showed a significant improvement in five domains (Learning and memory, abstraction/executive functioning, verbal fluency, attention/working memory, and Functional ($P < 0.05$) in each)
Hossain et al. (2017)	The potential of computerised cognitive training on HIV-associated neurocognitive disorder: A case comparison study	-USA -Case comparison -3	Cognitive training (10 h of SOP training, or 20 h of SOP training.)	Neuropsychological battery testing 7 cognitive domains	Only the participant who received 20 h of SOP training no longer met the criteria of HAND, post-test, as indicated by a 1-point improvement in his clinical rating.
Casaletto et al. (2016)	Abbreviated goal management training shows preliminary evidence as a neurorehabilitation tool for HIV-associated neurocognitive disorders among substance users	-USA -RCT -90	Meta-cognitive & goal management training	Brief neuropsychological battery testing 3 cognitive domains	Post hoc analyses showed that GMT and GMT + Meta-cognition groups demonstrated small benefits ($d = 0.20$–.27) compared to the control arm but did not differ from one another (ds < .10).

Table 2. Sociodemographic characteristics of the study participants from the reviewed articles on rehabilitation options for cognitive impairment among PLWHIV.

Study ID	Sample size	Age	Sex	Education	Race
		Mean ± SD	(% Male)	(Years)	(% White)
CE studies (Interv.)					
Vance et al. (2012)	46	51.06 ± 7.29	34 (73.9)	13.23(2.49)	27(58.7)
Towe et al. (2017)	21	47.74 ± 10.69	16(76.2)	13.34(2.30)	3 (9.5)
Livelli et al. (2015)	32	48.75 ± 10.30	8(25)	9.5(3.45)	30(93.8)
Casaletto et al. (2016)	90	49.50 ± 10.3	80(88.9)	13.17(2.60)	50(55.6)
Bai et al. (2018)	28	NR	NR	NR	NR
Hossain et al. (2017)	3	27.85 ± 4.68	0(0.00)	12.67(1.53)	0(0.0)
PA studies (Interv)					
Baigis et al. (2002)	99	37(rng=24-61)	79(79.8)	NR	32(32.3)
Robins et al. (2006)	59	42.3 ± 8.3	35(59.3)	NR	11 (19)
Fillipas et al. (2006)	40	43.5 ± 8.85	NR	NR	38(95)
Galantino et al. (2005)	38	NR	NR	NR	NR
Brown et al. (2016)	92	51.5 ± 9.6	75(81.5)	NR	65(70.7)
Schlabe et al. (2017)	13	42(27–50)	12(92.3)	NR	NR
McDermott et al. (2017)	11	43.50 ± 7.50	8(72.7)	NR	NR
PA studies (Non interv.)					
Dufour et al. (2018)	235	49.30 ± 9.80	172 (73%)	13.3 (3.1)	139(59.0)
Dufour et al. (2013)	335	47.70 ± 10.50	246 (74.3)	13(3.2)	172 (51.3)
Fazeli et al. (2014)	139	48.20 ± 10.03	111(79.86)	13.85(2.33)	83(59.7)
Fazeli et al. (2015)	100	58.20 ± 6.50	88 (88)	14.3(2.6)	82 (82)
Mapstone et al. (2013)	37	58.92 ± 5.62	30(81.8)	13.51(3.01)	27(73)
Monroe et al. (2017)	601	38.10±NR	NR	NR	356(59.4)
Chow et al. (2019)	998	51.5 ± 8.0	790(80)	14(12-16)†	485(49.0)
Ortega et al. (2015)	70	42.3 ± 16.40	65(16.4)	13.3(2.65)	52(74.3)
Grand total	2795	47.02 ± 8.23	1683(60.2)	12.88(2.75)	1517(54.3)

CE: cognitive exercise, PA: physical activity; Qlty: quality; II: insufficient information; rng: range; †: Median (Interquartile range).

Table 3. Assessment of methodological quality.

Authors	Are the participants representative of the target population?	Are measurements appropriate regarding both the outcome and intervention (or exposure)?	Are there complete outcome data?	Are the confounders accounted for in the design and analysis?	During the study period, is the intervention administered (or exposure occurred) as intended?
CE studies (Interv.)					
Vance et al. (2012)	YES	NO	YES	YES	YES
Towe et al. (2017)	YES	NO	YES	YES	YES
Livelli et al. (2015)	YES	NO	YES	YES	YES
Casaletto et al. (2016)	YES	YES	YES	YES	YES
Bai et al. (2018)	YES	NO	NO	NOT CLEAR	YES
Hossain et al. (2017)	YES	NO	YES	NA	YES
PA studies (Interv)					
Baigis et al. (2002)	YES	NO	YES	YES	YES
Robins et al. (2006)	YES	NO	NOT CLEAR	NOT CLEAR	YES
Fillipas et al. (2006)	NO	NO	YES	YES	YES
Galantino et al. (2005)	NO	NO	YES	YES	YES
Brown et al. (2016)	NO	NO	NOT CLEAR	NOT CLEAR	YES
Schlabe et al. (2017)	NO	NO	NO	NOT CLEAR	YES
McDermott et al. (2017)	NO	NO	YES	NO	NO

	Is the sampling strategy relevant to address the research question?	Is the sample representative of the target population?	Are the measurements appropriate?	Is the risk of nonresponse bias low?	Is the statistical analysis appropriate to answer the research question?
PA studies (Non interv.)					
Dufour et al. (2018)	NO	YES	YES	YES	YES
Dufour et al. (2013)	NO	YES	YES	YES	YES
Fazeli et al. (2014)	NO	YES	YES	YES	YES
Fazeli et al. (2015)	NO	NOT CLEAR	YES	YES	YES
Mapstone et al. (2013)	NO	NO	YES	YES	YES
Monroe et al. (2017)	NO	YES	YES	YES	YES
Chow et al. (2019)	YES	YES	YES	YES	YES
Ortega et al. (2015)	NO	NO	YES	YES	YES

Addition Test, while Grooved Pegboard constitutes the most important test for motor function.

Putative rehabilitative intervention options for HAND

We identified two potential rehabilitation interventions namely 'cognitive exercise' (Bai et al., 2018; Hossain et al., 2017; Livelli et al., 2015; Towe, Patel, & Meade, 2017; Vance et al., 2012, 2019) and 'physical activity'. The physical activity studies included seven interventional studies (Baigis et al., 2002; Brown, Claffey, & Harding, 2016; Fillipas, Oldmeadow, Bailey, & Cherry, 2006; Galantino et al., 2005; McDermott et al., 2017; Robins et al., 2006; Schlabe et al., 2017) and eight high quality observational studies (Chow et al., 2019; Dufour et al., 2013, 2018; Fazeli et al., 2014, 2015; Mapstone et al., 2013; Monroe et al., 2017; Ortega et al., 2015). All the studies reporting the use of cognitive exercise for cognitive function in PLWHIV reported significant positive post-training outcomes, whereas 33% of physical activity intervention studies reported significant improvements. For the physical activity intervention, treatment parameters included 'terms of duration', 'exercise lasted for 20–150 min per session', and 'exercise period of 2 months to 12 months'. Lower and upper exercise intensity ranges were 40-75HRM and 70-85HRM, respectively. Exercise types were mainly a combination of aerobic, resistance and balance exercises. Improvement in post-treatment outcome was reported in only one of the physical activity interventional studies (Fillipas et al., 2006). Unlike in physical activity intervention, treatment dosage in cognitive training studies is typically reported in number of hours of training engaged. Of the studies that reported treatment dosage, most employed 10 h of training, usually in 1-hour increments. Significant changes were reported for the cognitive domains including speed of information processing (Hossain et al., 2017; Vance et al., 2012), attention/working memory (Bai et al., 2018; Livelli et al., 2015; Towe et al., 2017), abstraction/executive function (Bai et al., 2018; Livelli et al., 2015), learning and memory (Livelli et al., 2015) and activities of daily living (ADL) (Casaletto et al., 2016; Livelli et al., 2015; Vance et al., 2012). Cognitive exercise studies focussed on PLWHIV who were cognitively impaired unlike the physical activity studies in which participants were cognitively intact PLWHIV. Cognitive exercise/training included speed of information training (Double Decision (UFOV), Eye for Detail (eye movement), Hawk Eye (visual accuracy), Target Tracker (multiple object tracker), Visual Sweeps (fundamental SOP)), memory training modules from PSSCogRehab, Time Pressure Management, Attention Process Training Task, Visual-verbal memory and learning, Visual-verbal memory and learning training, Errorless Learning, Process-Oriented Memory Learning, Metacognitive Strategy Training & Goal Management Training, Metacognitive Awareness, ERICA software comprising nine computer-based exercises aimed at improving five cognitive domains. Physical activity in most studies was unstructured, and where structured, exercises included combined aerobic, resistance exercise, manual therapy or Tai chi sessions. Improvement in post-treatment outcome was reported in only one of the physical activity interventional studies (Fillipas et al., 2006).

Discussion

In this scoping paper, all studies that met the eligibility criteria were reviewed irrespective of study characteristics such as sample size and comparison group. Our findings demonstrate two rehabilitation interventions for HAND namely psycho-cognitive training and physical activity. While cognitive function improved in 33% of the physical activity studies, cognitive exercise improved cognitive function in all seven studies. The improved cognitive function after cognitive exercise for PLWHIV is consistent with the results of a recent systematic review (Vance et al., 2019). However, we noticed that three of the six articles on cognitive function reported improvements in only one cognitive domain (Hossain et al., 2017; Towe et al., 2017; Vance et al., 2012), querying their clinical relevance. According to the Frascati criteria, cognitive impairment in PLWHIV is defined as sub-optimal performance in at least two cognitive domains with or without loss of independence in daily activities (Anitori et al., 2007; Yakasai et al., 2015; Yusuf et al., 2017). Hence, a clinically relevant improvement in cognitive functioning among PLWHIV would require improvements in at least two cognitive domains. Vance et al. (2012) examined only one cognitive domain (speed of information processing) but reported both improved ADL and information processing speed, while the other two studies (Hossain et al., 2017; Towe et al., 2017) used a comprehensive neuropsychological battery, thus further scrutiny of their clinical relevance is warranted. Unfortunately, we could not attribute this variance to methodological challenges such as sample size limitations and lack of adequate comparison groups as all studies in which quality appraisal was conducted were above average. Notably, most of the studies on cognitive exercised used 10 h of training which is a typical dose of intervention (Rebok et al., 2014). However, Lampit, Hallock, and Valenzuela (2014) argues that the optimal therapeutic dose of cognitive training is between 10 and 20 h, beyond which, the therapeutic benefit is reduced. This is corroborated by Vance et al. (2018), in which a reversal of HAND was observed after receiving 20 h of SOP training. Others suggest that improvements were only observed in the areas in which training occurs (Hossain et al., 2017; Towe et al., 2017; Vance et al., 2012), which is referred to as a near-transfer effect (Vance et al., 2019). However, Vance et al. (2021) highlighted the paucity of a 'far-transfer effect' as a major challenge facing cognitive training in their study, which was observed in an above average study (Vance et al., 2012). Far-transfer effect is a phenomenon in which cognitive training results in improved non-cognitive outcome such as the timed instrumental activities of daily living (Vance et al., 2019). Interestingly, there is a paucity of data surrounding a generic cognitive exercise intervention. Since HAND is a complex behavioural problem that impact more than two cognitive domains (Anitori et al., 2007), there is need for developing a more generic cognitive rehabilitation intervention that is capable of dealing with HAND irrespective of the domains affected. Our review data highlights that cognitive exercises hold a promise for the treatment and rehabilitation of HAND. However, to our knowledge, there is no study to date that investigated the putative role of cognitive training in prevention of HAND, which is a prevalent mental health challenge experienced by PLWHIV (Nweke et al., 2021; Wang et al., 2020). Future research should explore areas surrounding the relationship between dose and far-transfer effect; the effects of spacing of treatment sessions on effectiveness of cognitive training as well as examining the neuroprotective roles of cognitive training and their efficacy in promotion of cognitive functioning and prevention of cognitive disorder among PLWHIV. We also recommend a comprehensive meta-analytic approach to investigating the effects of cognitive training on cognitive and non-cognitive health outcomes.

All the observational studies reviewed on physical activity reported positive outcomes, but most of the intervention studies did not demonstrate improved cognitive function for cognitively intact PLWHIV. To our knowledge, there was no other systematic review. It is possible that the lack of any significant improvement in cognitive function after physical therapy interventions may be due to a lack of comprehensive neuropsychological testing, use of cognitively intact subjects and failure to control for pre-exercise physical activity levels. This collaborate the saying 'he that is not sick need no a physician' (*New Living Translation*

Bible, 1996, Mark 2:17). All clinical trials should employ comprehensive neuropsychological testing, especially because HAND is difficult to diagnose (Anitori et al., 2007). Although physical activity is widely advocated for improving cognitive function, or overall health, in PLWHIV (Vance, Fazeli, Moneyham, Keltner, & Raper, 2013; Vance et al., 2012), we could not find any evidence supporting this advocacy. Notably, none of the studies included in this review was conducted in an African population, hence, the position of sub-Saharan Africa vis-à-vis HAND rehabilitation remains unclear. Thus far, all the interventional physical activity studies were only conducted among PLWHIV with no known history or diagnosis of HAND, highlighting the paucity of data in this area. It appears that one of the challenges facing the field of neuroHIV is the lack of knowledge on the part of physical activity professionals to diagnose HAND. There was no attempt to diagnose HAND in any of the physical activity studies instead simple measures of cognitive impairment were used. To achieve the objective of establishing the interaction of physical activity interventions and HAND, there is need for training of physical activity professionals working with PLWHIV on diagnosis of neuroHIV conditions. Further, research is required to investigate the effects of various physical activity interventions on HAND, and to establish the optimal therapeutic dose of exercise for both prevention and rehabilitation of HAND. Moreover, studies investigating the relationship between exercise-induced cardiovascular fitness and cognitive performance among PLWHIV is essential to improve our understanding of the putative mechanism by which physical activity impacts HAND.

Strength and limitations

One notable strength of this scoping review is the use of five databases hence the minimal chance of missing any studies. The application of quantitative synthesis, where applicable, adds to the strength of the study thus allowing inference to be drawn, albeit cautiously. The fact that we could not assess the quality of three studies (Bai et al., 2018; Robins et al., 2006; Towe et al., 2017) because of insufficient important information may negatively influence our findings.

Clinical implications of review findings

Although the findings need to be re-examined through systematic review and meta-analysis, we found the findings of this scoping review of clinical relevance. Individuals living with HAND on ART should be exposed to cognitive rehabilitation exercises as early as possible. What remains elusive is who is qualified to administer the intervention. People living with HAND are numerous in number hence, in addition to clinical psychologists, health professionals working with people living with HIV including physicians, physiotherapists and nurses may be qualified to administer the intervention, provided they have post-qualification certification to do so. We recommend that training be provided through group classes to minimise the burden of long and intensive cognitive rehabilitation interventions.

Conclusion

There exists a positive relationship between cognitive performance and type of intervention, with cognitive rehabilitation exercises, unlike physical activity interventions, showing improved post-treatment cognitive performance. Psycho-cognitive training is a profitable and cost-effective rehabilitation intervention for HIV-associated cognitive impairment; although more well-designed RCTs are needed to establish effectiveness. We could not find sufficient evidence to support physical activity as a rehabilitation intervention for cognitive impairment in PLWHIV, although physical activity does improve overall health. Clinical trials are needed to test the efficacy of physical activity interventions for HIV-associated cognitive impairment.

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References

Alford, K., & Vera, J. H. (2018). Cognitive impairment in people living with HIV in the ART era: A review 2018. *British Medical Bulletin*, *127*(1), 55–68. doi:10.1093/bmb/ldy019

Alkali, N. H., Bwala, S. A., Nyandaiti, Y. W., & Danesi, M. A. (2013). NeuroAIDS in sub-Saharan Africa: A clinical review. *Annals of African Medicine*, *12*(1), 1–10. doi:10.4103/1596-3519.108242

Anitori, A., Arendt, G., Becker, J. T., Brew, B. J., Byrd, D. A., Cherner, M., … Wojna, V. E. (2007). Updated research nosology for HIV-associated neurocognitive disorders. *Neurology*, *69*, 1789–1799. doi:10.1212/01.WNL.0000287431.88658.8b

Bai, F., Allegrini, M., Falcinella, C., Strada, I., Borghi, L., Merlini, E., … Marchetti, G. (2018). Efficacy of a computerized cognitive rehabilitation training in improving HIV-associated neuro-cognitive disorders. *Journal of the International AIDS Society*, *21*(8), e25187. doi:10.1002/jia2.25187

Baigis, J., Korniewicz, D. M., Chase, G., Butz, A., Jacobson, D., & Wu, A. W. (2002). Effectiveness of a home-based exercise intervention for HIV-infected adults: A randomized trial. *Journal of the Association of Nurses in AIDS Care*, *13*(2), 33–45. doi:10.1016/S1055-3290(06)60199-4

Banks, L. M., Zuurmond, M., Ferrand, R., & Kuper, H. (2017). Knowledge of HIV-related disabilities and challenges in accessing care: Qualitative research from Zimbabwe. *PloS one*, *12*(8), e0181144. doi:10.1377/journal.pone.0181144

Becker, J. T., Dew, M. A., Aizenstein, H. J., Lopez, O. L., Morrow, L., Saxton, J., … Tarraga, L. (2012). A pilot study of the effects of internet-based cognitive stimulation on neuropsychological function in HIV disease. *Disability and Rehabilitation*, *34*(21), 1848–1852. doi:10.3109/09638288.2012.667188

Brown, D., Claffey, A., & Harding, R. (2016). Evaluation of a physiotherapy-led group rehabilitation intervention for adults living with HIV: Referrals, adherence and outcomes. *AIDS Care*, *28*(12), 1495–1505. doi:10.1080/09540121.2016.1191611

Casaletto, K. B., Moore, D. J., Woods, S. P., Umlauf, A., Scott, J. C., & Heaton, R. K. (2016). Abbreviated goal management training shows preliminary evidence as a neuro-rehabilitation tool for HIV-associated neurocognitive disorders among substance users. *The Clinical Neuropsychologist*, *30*(1), 107–130. doi:10.1080/13854046.2015.1129437

Chetty, V., Maddocks, S., Cobbing, S., & Hanass-Hancock, J. (2018). A study protocol "saving futures: Developing an integrated model of rehabilitation and paediatric HIV care to foster success at school". *Pilot and Feasibility Studies*, *4*(1), 178. doi:10.1186/s40814-018-0372-7

Chow, F. C., Makanjuola, A., Wu, K., Berzins, B., Kim, K. A., Ogunniyi, A., … Taiwo, B. O. (2019). Physical activity is associated with lower odds of cognitive impairment in women but not men living with human immunodeficiency virus infection. *The Journal of Infectious Diseases*, *219*(15), 264–274. doi:10.1093/infdis/jiy503

Clifford, D. B. (2017). HIV-associated neurocognitive disorder. *Current Opinion in Infectious Disease*, *30*(1), 117–122. doi:10.1097/QCO.0000000000000328

Clifford, D. B., & Ances, B. M. (2013). HIV-associated neurocognitive disorder (HAND). *Lancet Infectious Disease*, *13*(11), 976–986. doi:10.1016/S1473-3099(13)70269-X

Deeks, S. G., Lewin, S. R., & Havlir, D. V. (2013). The end of AIDS: HIV infection as a chronic disease. *Lancet*, *382*(9903), 1525–1533. doi:10.1016/S0140-6736(13)61809-7

Devendra, A., Makawa, A., Kazembe, P. N., Calles, N. R., & Kuper, H. (2013). HIV and childhood disability: A case-controlled study at a paediatric antiretroviral therapy centre in Lilongwe, Malawi. *PloS one*, *8*(12), e84024. doi:10.1371/journal.pone.0084024

Dufour, C. A., Marquine, M. J., Fazeli, P. L., Henry, B. L., Ellis, R. J., Grant, I., … HNRP Group (2013). Physical exercise is associated with less neurocognitive impairment among HIV-infected adults. *Journal of Neurovirology*, *19*(5), 410–417. doi:10.1007/s13365-013-0184-8

Dufour, C. A., Marquine, M. J., Fazeli, P. L., Umlauf, A., Henry, B. L., Zlatar, Z., … HNRP Group (2018). A longitudinal analysis of the impact of physical activity on neurocognitive functioning among HIV-infected adults. *AIDS and Behaviour*, *22*(5), 1562–1572. doi:10.1007/s10461-016-1643-z

Fazeli, P., Woods, S., Heaton, R., Umlauf, A., Gouaux, B., Rosario, D., … HNRP Group (2014). An active lifestyle is associated with better neurocognitive functioning in adults living with HIV infection. *Journal of Neurobiology*, *20*(3), 233–242. doi:10.1007/s13365-014-0240-z

Fazeli, P. L., Marquine, M. J., Dufour, C., Henry, B. L., Montoya, J., Gouaux, B., … HNRP Group. (2015). Physical activity is associated with better neurocognitive and everyday functioning among older adults with HIV disease. *AIDS and Behavior*, *19*(8), 1470–1477. doi:10.1007/s10461-015-1024-z

Fillipas, S., Oldmeadow, L. B., Bailey, M. J., & Cherry, C. L. (2006). A six-month, supervised, aerobic and resistance exercise program improves self-efficacy in people with human immunodeficiency virus: A randomised controlled trial. *Australia Journal of Physiotherapy*, *52*(3), 185–190. doi:10.1016/s0004-9514(06)70027-7

Galantino, M.L., Shepard, K., Krafft, L., Laperriere, A., Ducette, J., Sorbello, A., … Farrar, J. T. (2005). The effect of group aerobic exercise and T'ai chi on functional outcomes and quality of life for persons living with acquired immunodeficiency syndrome. *Journal of Alternative & Complementary Medicine*, *11*(6), 1085–1092. doi:10.1089/acm.2005.11.1085

Guaraldi, G., Orlando, G., Zona, S., Menozzi, M., Carli, F., Garlassi, E., … Palella, F. (2011). Premature age-related comorbidities among HIV-infected persons compared with the general population. *Clinical Infectious Diseases*, *53*(11), 1120–1126. doi:10.1093/cid/cir627

Hawkins, K. L., Brown, T. T., Margolick, J. B., & Erlandson, K. M. (2017). Geriatric syndromes: New frontiers in HIV and sarcopenia. *Aids (london, England)*, *31*(2), 137–146. doi:10.1097/QAD.0000000000001444

Hong, Q.N., Pluye, P., Fàbregues, S., Bartlett, G., Boardman, F., Cargo, M., … Vedel, I. (2018). *Mixed methods appraisal tool (MMAT), version 2018*. Canadian Intellectual Property Office, Industry Canada. Retrieved from https://mixedmethodsappraisaltoolpublic.pbworks.com/

Hossain, S., Fazeli, P. L., Tende, F., Bradley, B., McKie, P., & Vance, D. E. (2017). The potential of computerized cognitive training on HIV-associated neurocognitive disorder: A case comparison study. *Journal of Association of Nurses in AIDS Care*, *28*(6), 971–976. doi:10.1016/j.jana.2017.06.011

Kumar, S., Himanshu, D., Tandon, R., Atam, V., Sawlani, K. K., & Verma, S. K. (2019). Prevalence of HIV-associated neurocognitive disorder using modified mini mental state examination and its correlation with CD4 counts and anti-retroviral therapy. *Journal of Association of Physicians India*, *67*(4), 47–51.

Lampit, A., Hallock, H., & Valenzuela, M. (2014). Computerized cognitive training in cognitively healthy older adults: A systematic review and meta-analysis of effect modifiers. *PLoS Medicine*, *11*(11), e1001756. doi:10.1371/journal.pmed.1001756

Levac, D., Colquhoun, H., & O'Brien, K. K. (2010). Scoping studies: Advancing the methodology. *Implementation Science*, *5*, Article 69. doi:10.1186/1748-5908-5-69

Livelli, A., Orofino, G.C., Calcagno, A., Farenga, M., Penoncelli, D., Guastavigna, M., … Pia , L. (2015). Evaluation of a cognitive rehabilitation protocol in HIV patients with associated neurocognitive disorders: Efficacy and stability over time. *Frontier of Behavioural Neuroscience*, *9*, Article 306. doi:10.3389/fnbeh.2015.00306

Mapstone, M., Hilton, T. N., Hongmei, Y., Guido, J. J., Luque, A. E., Hall, W. J., … Shah, K. (2013). Poor aerobic fitness may contribute to cognitive decline in HIV-infected older adults. *Aging & Disease*, *4*(6), 311–319. doi:10.14336/AD.2013.0400311

McDermott, A., Zaporojan, L., McNamara, P., Doherty, C.P., Redmond, J., Forde, C., … Ber gin, C. (2017). The effects of a 16-week aerobic exercise programme on cognitive function in people living with HIV. *AIDS Care*, *29*(6), 667–674. doi:10.1080/09540121.2016.1263723

Modi, G., Mochan, A., & Modi, M. (2018). Neurological manifestations of HIV. In O. Samuel (Ed.), *Advances in HIV and AIDS control*. IntechOpen. doi:10.5772/intechopen.80054

Monroe, A. K., Zhang, L., Jacobson, L. P., Plankey, M. W., Brown, T. T., Miller, E. N., … Sacktor, N. C. (2017). The association between physical activity and cognition in men with and without HIV infection. *HIV Medicine*, *18*(8), 555–563. doi:10.4102/sajhivmed.v18i1.776

Morgan, E. E., Woods, S. P., & Grant, I. (2012). The HIV neurobehavioral research program (HNRP) group. Intra-individual neurocognitive variability confers risk of dependence in activities of daily living among HIV-seropositive individuals without HIV-associated neurocognitive disorders. *Archive Clinical Neuropsychology*, *27*(3), 293–303. doi:10.1093/arclin/acs003

Nweke, M. C., Mshunqane, M., Govender, N., & Akinpelu, O. A. (2021). Effects of physical activity on cognition in people living with HIV: A preliminary synthesis. *African Journal for Physical Activity and Health Sciences*, *27*(1), 1–22. doi:10.37597/ajphes.2021.27.1

Nweke, M.C., Okemuo, A.J., Uduonu, E.M., Ugwu, P.I., Nwachukwu, C., Mshunqane N. (20 21). Meta-analysis of factors affecting prevalence estimates of HIV-associated neurocognitive disorder in sub-Saharan Africa. *South African Journal of Science*, *117*(9/10), Art. #8575. doi:10.17159/sajs.2021/8575

O'Brien, K.K., Solomon, P., Trentham, B., MacLachlan, D., MacDermid, J., Tyan, A., … Zac k, E. (2014). Evidence-informed recommendations for rehabilitation with older adults living with HIV: A knowledge synthesis. *BMJ Open*, *4*(5), e004692. doi:10.1136/bmjopen-2013-004692

Ortega, M., Baker, L. M., Vaida, F., Paul, R., Basco, B., & Ances, B. M. (2015). Physical activity affects brain integrity in HIV + individuals. *Journal of International Neuropsychological Society*, *21*(10), 880–889. doi:10.1017/S1355617715000879

Rebok, G. W., Ball, K., Guey, L. T., Jones, R. N., Kim, H. Y., King, J. W., … ACTIVE Study Group. (2014). Ten-year effects of the advanced cognitive training for independent and vital elderly cognitive training trial on cognition and everyday functioning in older adults. *Journal of the American Geriatrics Society*, *62*(1), 16–24.

Robins, J.W., McCain, N.L., Gray, D.P., ElswickJr, R.K., Walter, J.M., McDade, E. (2006). Research on psychoneuroimmunology: Tai chi as a stress management approach for individuals with HIV disease. *Applied Nursing Research*, *19*(1), 2–9. doi:10.1016/j.apnr.2005.03.002

Schlabe, S., Vogel, M., Boesecke, C., Schwarze-Zander, C., Rockstroh, J. K., Korner, C., & Wasmuth, J. C. (2017). Moderate endurance training (marathon-training) – effects on immunologic and metabolic parameters in HIV-infected patients: The 42 KM cologne project. *BMC Infectious Disease*, *17*, 550. doi:10.1186/s12879-017-2651-y

Society of Neuroscientist of Africa. (2015). *The 12th international conference of society of neuroscientists of Africa (SONA)*. Retrieved from https://sonafrica.info/component/content/article/84-adverts/222-ilcb-blri

Thakur, K. T., Boubour, A., Saylor, D., Das, M., Bearden, D. R., & Birbeck, G. L. (2019). Global HIV neurology: A comprehensive review. *AIDS*, *33*(2), 163–184. doi:10.1097/QAD.0000000000001796

The Holy Bible. (1996). New living translation. *Mark*, *2*, 17.

The Joanna Briggs Institute. (2015). The Joanna Briggs Institute reviewers' manual: 2015 edition / supplement. Retrieved from https://www.Joannabriggs.org

Towe, S. L., Patel, P., & Meade, C. S. (2017). The acceptability and potential utility of cognitive training to improve working memory in persons living with HIV: A preliminary randomized trial. *Journal of Association of Nurses in AIDS Care*, *28*(4), 633–643. doi:10.1016/j.jana.2017.03.007

Tricco, A. C., Lillie, E., Zarin, W., O'Brien, K. K., Colquhoun, H., Levac, D., … Straus, S. E. (2018). PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. *Annals of Internal Medicine*, *169*(7), 467–473. doi:10.7326/M18-0850

U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion. (2010). *National Action Plan to Improve Health Literacy*. Washington, DC: Author.

Vance, D. E., Fazeli, P. L., Azuero, A., Wadley, V. G., Raper, J. L., & Ball, K. K. (2021). Can individualized-targeted computerized cognitive training benefit adults with HIV-associated neurocognitive disorder? The Training on Purpose Study (TOPS). *AIDS and Behavior*. doi:10.1007/s10461-021-03230-y

Vance, D. E., Fazeli, P. L., Cheatwood, J., Nicholson, W. C., Morrison, S. A., & Moneyham, L. D. (2019). Computerized cognitive training for the neurocognitive complications of HIV infection: A systematic review. *Journal of Association of Nurses in AIDS Care*, *30*(1), 51–72. doi:10.1097/JNC.0000000000000030

Vance, D. E., Fazeli, P. L., Moneyham, L., Keltner, N. L., & Raper, J. L. (2013). Assessing and treating forgetfulness and cognitive problems in adults with HIV. *Journal of Association of Nurses in AIDS Care*, *24*(1), 40–60. doi:10.1016/j.jana.2012.03.006

Vance, D. E., Fazeli, P. L., Ross, L. A., Wadley, V. G., & Ball, K. K. (2012). Speed of processing training with middle-age and older adults with HIV: A pilot study. *Journal of Association of Nurses in AIDS Care*, *23*(6), 500–510. doi:10.1016/j.jana.2012.01.005

Vance, D. E., Jensen, M., Tende, F., Raper, J. L., Morrison, S., & Fazeli, P. L. (2018). Individualized-targeted computerized cognitive training to treat HIV-associated neurocognitive disorder: An interim descriptive analysis. *The Journal of the Association of Nurses in AIDS Care*, *29*(4), 604–611. doi:10.1016/j.jana.2018.04.005

Wang, Y., Liu, M., Lu, Q., Farrell, M., Lappin, J. M., Shi, J., … Bao, Y. (2020). Global prevalence and burden of HIV-associated neurocognitive disorder: A meta-analysis. *Neurology*, *95*(19), e2610–e2621. doi:10.1212/WNL.0000000000010752

Weber, E., Blackstone, K., & Woods, S. P. (2013). Cognitive neurorehabilitation of HIV-associated neurocognitive disorders: A qualitative review and call to action. *Neuropsychology Review*, *23*(1), 81–98. doi:10.1007/s11065-013-9225-6

World Health Organization. (2019). *Rehabilitation*. Retrieved from https://www.who.int/news-room/fact-sheets/detail/rehabilitation

Yakasai, A. M., Gudaji, M. I., Muhammad, H., Ibrahim, A., Owolabi, L. F., Ibrahim, D. A., … Habib, A. G. (2015). Prevalence and correlates of HIV-associated neurocognitive disorders (HAND) in northwestern Nigeria. *Neurology Research International*, *2015*, 486960. doi:10.1155/2015/486960

Yusuf, A.J., Hassan, A., Mamman, A.I., Muktar, H.M., Sulieman, A. M., Baiyewu, O. (2017). Prevalence of HIV-associated neurocognitive disorder (HAND) among patients attending a tertiary health facility in northern Nigeria. *Journal of International Association of Providers of AIDS Care*, *16*(1), 48–55. doi:10.1177/2325957414553839