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Feasibility and potential benefits of a structured exercise program on cognitive performance in HIV

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ABSTRACT

Although exercise has been shown to improve cardiorespiratory and metabolic outcomes in people with HIV, its effect on cognitive ability remains understudied. Our study aimed to estimate the feasibility and efficacy potential of a 12-week aerobic and resistance training program on cognitive and physical performance outcomes. This is an externally controlled, two time-point, feasibility study within a larger study using a cohort multiple randomized controlled design yielding 3 groups: intervention group; comparison group and refusers. The intervention consisted of high-intensity interval training and resistance exercises 3 days/week. Specific feasibility and brain health outcomes were evaluated. Cognitive ability was ascertained by the Brief Cognitive Ability Measure (B-CAM) in all three groups. Standardized tests of physical performance were performed in the intervention group. Effect size, 95% confidence intervals, responder status analyses and reliable change indices were computed. Adherence to the intervention schedule and acceptability outcomes were good. There was no reliable change on B-CAM in the exercise group. Most physical performance measures benefited from the exercise training (effect sizes: 0.2 – 1.5). Although the 12-week exercise program improved physical capacity, it did not yield gains in cognitive ability in HIV. Further research is required to determine the exercise parameters that could benefit cognition.

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Introduction

The prognosis for people living with HIV in resource-rich settings is optimistic owing to the widespread availability and use of combined anti-retroviral therapy (cART). Remarkably, the post-cART era has added approximately 43.1 years to the life of an individual affected with HIV (Gueler et al., 2017). Despite the elimination of the detectable virus in the plasma with cART, HIV-associated neurocognitive disorders (HAND) continue to escalate with these gains in life expectancy (Fazeli et al., 2015).

Previous meta-analyses have reported benefits of exercise in improving cardiopulmonary, body composition, and musculoskeletal outcomes, in addition to various aspects of quality of life in HIV (Gomes-Neto et al., 2015). The evidence supporting the association of physical activity and cognition in HIV comes substantially from cross-sectional studies (Dufour et al., 2013; Fazeli et al., 2015; Ortega et al., 2015). Most exercise intervention studies have not shown improvement in the cognitive outcomes in HIV. One randomized controlled trial (RCT; Fillipas et al., 2006) of 6 months of combined aerobic and resistance training showed a between-group difference of 14 points [95% confidence intervals (CI): 0.7–27.3] on the Cognitive sub-scale of Medical Outcomes Study (MOS) HIV Health Survey.

A meta-analysis (Kelly et al., 2014) in healthy older adults found that resistance training versus stretching improved measures of verbal reasoning [standardized mean difference (SMD) = 3.16; 95% confidence intervals (CI): 1.07–5.24]. In mild cognitive impairment (MCI), a systematic review covering 7 clinical trials concluded that exercise can yield a positive influence on cognitive abilities, particularly in global cognition, executive function or attention in MCI (Öhman et al., 2014). One premise underlying this literature is that a sufficient dose of exercise that can benefit cardiovascular health needs to be delivered to induce changes in cognition. The exercise-mediated mechanisms underlying brain health include increased neurotrophin levels, better vascularization, enhanced synaptogenesis, and reduced chronic inflammation (Kern-Sanchez & McGough, 2013).

Exercise is an inexpensive intervention with widespread benefits to vascular and musculoskeletal health

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and few harms. Evidence for benefit to brain health and cognition would likely encourage adoption of exercise by people with HIV. This study on the feasibility of a structured exercise program in HIV+ individuals had two specific objectives: (a) to estimate the feasibility of a 12-week combined aerobic and resistance (power) exercise program; and (b) to estimate the extent to which participants changed in cognitive ability, physical performance, and other brain health outcomes (self-reported cognitive deficits, anxiety/depression, fatigue and motivation) after 12 weeks of training.

Methods

Study design

This is an externally controlled, two time-point, feasibility study within a larger study [Positive Brain Health Now (+BHN); Mayo et al., 2016] with a cohort multiple randomized controlled trial (cmRCT) (Relton et al., 2010) design. This design (see Figure 1), when operationalized for a single-arm (here of an exercise intervention), yielded three groups: (i) the intervention group, comprising all those approached and who agreed to enter; (ii) the refusers, comprising all those approached who declined entry; and (iii) a comparison group, comprising all eligible cohort participants who were not approached, and hence were not given the opportunity to accept or decline. The design and framework of this study was informed by the Consolidated Standards of Reporting Trials (CONSORT) guidelines for feasibility studies (Eldridge et al., 2016). It was registered at clinicaltrials.gov (ID: NCT03053817). All participants gave written informed consent.

Eligibility criteria

The eligibility criteria for the +BHN cohort have been described elsewhere (Mayo et al., 2016). Briefly, the target population was people aged ≥35 years, HIV+ for at least 1 year, and able to communicate adequately in either French or English. To be included, all participants had to identify that they were mostly sedentary (moderate level physical activity of 30 min duration less than twice a week or have limitations in performing vigorous activities, walking a kilometer, or climbing stairs). Excluded were people with a contraindication for exercise from cardiovascular or musculoskeletal co-morbidity as determined by the medical history and the Physical Activities Readiness Questionnaire (PAR-Q) (Thomas et al., 1992).

Intervention

The intervention was based on current recommendations that suggest exercise programs combining aerobic with resistance training yield optimal health benefits for people with HIV (Malita et al., 2005). High-intensity interval training (HIIT) (Billat, 2001) using elliptical machines was performed for 21 min including a three-minute warm-up and cool-down period [60% to 65% of maximum heart rate (MHR)]. The interval program lasted around 15 min with 30 s bursts of exercise at an intensity of 80–85% of the MHR (>17 on Borg Scale; Williams, 2017) followed by 1 min and 30 s of active recovery. Resistance training for major muscle groups (hamstrings, pectorals, quadriceps, and latissimus dorsi) at tempo 1–0–2–1 was carried out with weight machines in 2 sets of 12 repetitions and lasted 24 min. The resistance was set at 80% of the one-repetition maximum (1RM). To ensure progressive overload, resistance was enhanced when participants were able to perform more than 15 repetitions. This supervised 45-min exercise program was performed 3 times a week (on alternate days) at a research-based gym in groups of 4–5 participants. Participants received an honorarium of $103 to offset transportation costs and time spent in the evaluations.

Measurement strategy

The measurement strategy for this study has been outlined in Table 1.

Feasibility outcomes

The proportion of participants recruited was recorded. Adherence to the intervention schedule was estimated by the number of sessions attended out of the total 36 sessions. Good adherence was defined as completion of at least 29 (80%) of the prescribed sessions. Acceptability of the intervention was estimated by asking participants how much they enjoyed the exercise program on a scale of from 0 (did not enjoy at all) to 10 (enjoyed a lot). Participants were also asked before the exercise training how much they enjoyed exercise in general on the same scale. Additionally, the feedback was obtained from each participant at the end of the intervention with an open-ended format.

Brain health outcomes

The primary efficacy potential outcome was the Brief Cognitive Ability Measure (B-CAM) (Brouillette et al., 2015). This was part of the measurement platform in the parent study (+BHN; Mayo et al., 2016) and was captured 9 months apart. B-CAM is a performance-based measure that taps into the domains of executive function, memory, attention and language. Higher scores are indicative of better cognitive ability (Brouillette et al., 2015). A clinically meaningful change on B-

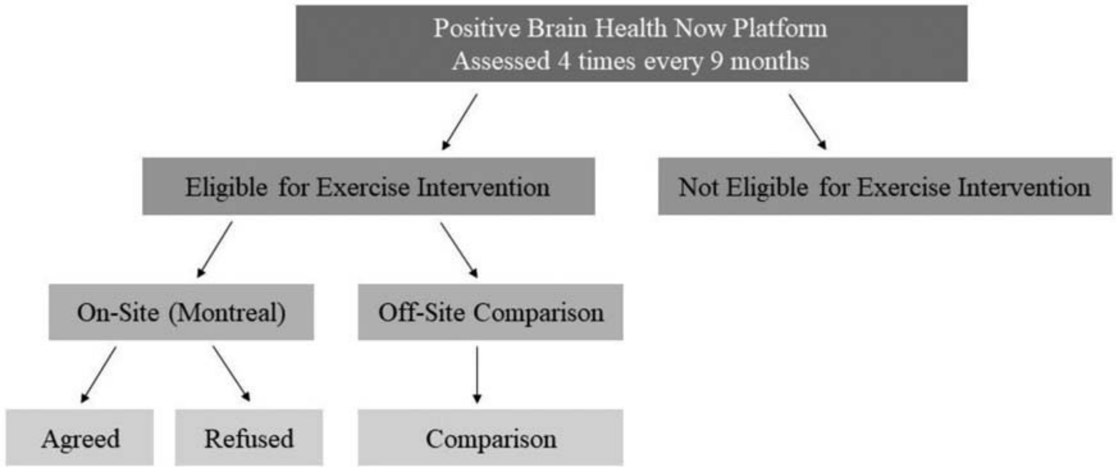

Figure 1. In the multi-site Cohort Multiple Randomized Controlled trial (cmRCT), platform refers to the measures used to fully characterize the cohort of people with HIV every 9 months. For the exercise intervention, eligible participants in the cohort were identified. The participants who were eligible in Montreal were approached in a random order and invited to take part in the intervention. Those who agreed formed the intervention group. The rest of the eligible participants outside Montreal served as the comparison group. An additional group comprising those approached from Montreal site but refused served to assess the degree of selection bias. The strength of this design is that it allows making comparisons between the participants in the sub-study (here exercise) with the eligible participants in the larger cohort in order to justify a larger, likely multi-site study.

CAM is equivalent to ½ a standard deviation (SD) (Norman et al., 2004).

Brain health indicators were also part of the platform and were measured at the same time points as the B-CAM. The exercise intervention took place in a 3-month period between the two 9-month apart assessments. Perceived Deficits Questionnaire (PDQ) was used to reflect every day cognitive challenges as reported by the participants themselves over the previous 4 weeks (Sullivan et al., 1990).

The brain health outcomes of fatigue and anxiety/depression were measured using the vitality subscale and mental health inventory (MHI), respectively from RAND-36; a generic measure of health status (Hays et al., 1993). The subscale scores range from 0 to 100, with greater scores representing better health status.

Table 1. Measurement strategy for efficacy potential of the 12-week exercise training.

Outcome	Measure
Primary Efficacy Potential Outcome (Platform measure, 2 assessments – 9 months apart)	
Cognitive ability	Brief Cognitive Ability Measure (B-CAM; 0–36)
Other Brain Health Outcomes (Platform, 2 assessments – 9 months apart)	
Self-reported cognitive deficits	Perceived Deficits Questionnaire (PDQ; 0–80)
Anxiety/Depression	RAND-36 Mental Health Inventory (MHI; 0–100)
Fatigue	RAND-36 Vitality (0–100)
Motivation	Motivation ladder (0–42)[a]
Exercise Specific Measures (0 and 12 weeks)	
Exercise capacity (kg/ml/min)	Step test
Functional walking capacity (m)	Six-Minute Walk Test (6MWT)
Seated leg power (W)	Power rig
Jump height (cm)	Vertical Jump test
Comfortable gait speed (m/s)	GAITRite (4m track)
Fast gait speed (m/s)	GAITRite (4m track)
Dual-task gait speed (m/s)	GAITRite and naming fruit (4m track)
Hand grip strength (kg)	Jamar dynamometer
Core strength (#)	Push-ups and partial curl-ups
Other Cognitive Outcomes (0 and 12 weeks)	
Verbal (categorical) fluency	Number of unique animals generated in 1 minute

[a]Motivation was elicited using three questions: (i) Are you always looking for something to do? (ii) Are you interested in learning new things? (iii) Do you have plans and goals for the future? The response options ranged from not at all, some and a lot. It has a Rasch-derived score ranging from 0 to 42 and higher scores indicate better motivation.

Exercise specific measures

The rest of the measures employed in this study were administered before and after the 12-week intervention only for the exercise group. Modified Canadian Aerobic Fitness Test (mCAFT) was used for predicting exercise capacity (Weller et al., 1993). For core strength, partial curl-ups and push-ups were performed, and upper limb strength was measured using a Jamar dynamometer. Jump height was measured using the vertical jump test. Standardized test procedures were followed as stipulated in the Canadian Physical Activity, Fitness and Lifestyle Approach (CPAFLA) manual. Lower limb muscle power was calculated using Nottingham Leg Extensor Power rig (Bassey & Short, 1990) in a seated position. Functional exercise capacity was determined with the Six-Minute Walk Test (6-MWT) (American Thoracic Society, 2002). Both comfortable and fast gait speed were measured using the instrumented walkaway system (GAITRite®). Participants walked comfortably on a 4-metre track in a straight line and the time taken (in seconds) to complete the 4-metre distance was monitored. This was followed by 4-metre walk at a fast pace.

For measuring dual-task gait speed, participants were instructed to name as many fruits as they could while concurrently walking on the 4-metre track in a straight line at a comfortable pace (Plummer & Iyigün, 2018). Verbal fluency was measured by instructing the participants to produce as many unique words as possible (in either French or English) within a specific category (i.e., animals) in 1 min in a seated position (Shao et al., 2014).

Sample size and analysis

This study was designed to identify the proportion of individuals with a cognitive response rather than calculating an average response for the primary efficacy potential outcome, i.e., B-CAM.

With the assumption that the change on B-CAM is drawn from a binomial distribution, 30 subjects in the intervention group would allow detection of a positive response at $p < .05$ if 7 or more persons achieve a response, assuming an expected probability of response with no intervention of 10% ($n = 3$) (stattrek.com binomial calculator). The extent to which the exercise participants changed after the 12-week intervention was estimated using a paired t-test for physical performance outcomes. Responsiveness was elicited in terms of standardized response mean (SRM; Terwee et al., 2003) and corresponding 95% CI were presented. To account for measurement error, the Reliable Change Index (RCI) was computed for specific outcomes (Estrada et al., 2019). Reliable change per group was defined by values larger than 1.645.

Results

A total of 27 participants completed the 12-week exercise program. Figure 2 shows the flow of participants in the exercise program.

Table 2 shows the characteristics of all three groups at baseline. The mean age of the people in the exercise group was 54.4 (SD 6.5) closely similar to that of the other groups: mean 52.2 (SD 8.2) for the comparison group and 53.8 (SD:8.1) for the refusers. Overall, there were more men than women in all groups reflecting the sex distribution of the entire cohort.

The median (IQR) of the ratings of perceived enjoyment for general exercise (received before the intervention) was high, at 8 (5–9). Adherence to the exercise training schedule was 85.2%. The program was well-received as shown by the ratings for the exercise enjoyment [median (IQR): 9 (8–10)]. No negative comments were received in the open-ended feedback obtained at the end of the intervention indicating good acceptability of the program.

Table 3 shows the extent of within-group change in the primary efficacy potential outcome, i.e., B-CAM, pre-and post-exercise training, for all three groups. Among the exercisers ($n = 27$), average change in B-CAM post-exercise was near 0 (mean: 0.2; SD: 3.3). 26% made a gain equivalent to 1/2 SD, 22% declined, and 52% remained unchanged. For the two comparison groups, the proportion making meaningful gains also exceeded the proportion declining. Based on reliable change indices, only 3.7% of the exercisers improved on B-CAM.

Table 4 shows the outcome of change in verbal fluency, comfortable gait speed and dual-task gait speed among the exercisers. Before and after the exercise program, the mean number of words produced in a minute were higher than the Canadian norms, i.e., 17. Although the majority (70%) of the participants exhibited no change in verbal fluency, 15% of the sample showed meaningful improvements (>5 words). However, when accounted for measurement error, only 3.7% of the sample seemed to have benefited. The reliable change observed in comfortable gait speed and dual-task gait speed was 30% and 11.1%, respectively in the exercise group.

Table 5 presents the results of the physical performance measures pre-and post-exercise training in the exercise group. The SRM was highest for partial curl-ups (1.5; 95% CI:1.1–2.3) and lowest for vertical jump height (0.2; 95% CI: −0.2–0.7).

Table 6 presents the pre-and post-exercise performance in the platform measures. Median and interquartile range (IQR) values have been presented for the MHI and Vitality scores. None of the platform measures in any of the groups benefited from the exercise training.

Discussion

This study was aimed at estimating the feasibility and efficacy potential of a 12-week structured exercise program to change cognitive performance in people living with HIV. The exercise program yielded gains in predicted aerobic capacity and physical performance (effect sizes ranging from 0.5 to 1.5) among the exercisers and hence had the potential to influence cognition. Despite this, little effect was shown on B-CAM as a reliable change was observed for only one person.

For the exercisers, the improvement of various cardiorespiratory and physical performance measures post-

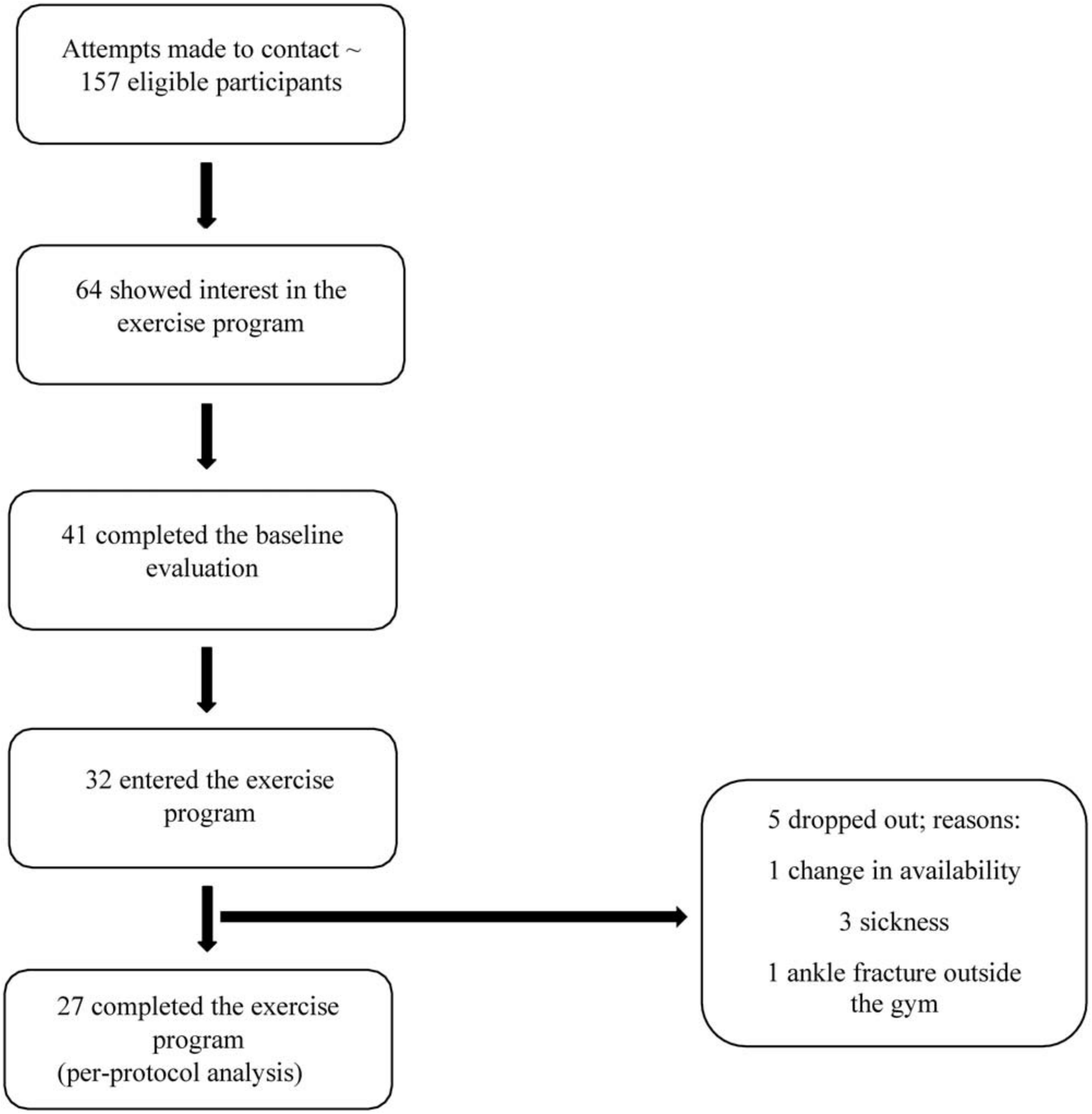

Figure 2. Flow of study participants into the exercise program.

training was in line with the extant literature in HIV (Chaparro et al., 2018; Gomes-Neto et al., 2015; O'Brien et al., 2016, 2017). A meta-analysis reported significant improvement in peak aerobic capacity by 4.8 ml/kg/min (95% CI: 2.95–6.0) and muscular strength based on 7 studies with a combined aerobic and resistance training program (ranging from 6 to 24 weeks) compared to non-exercising controls (Gomes-Neto et al., 2015). In our exercise group, there was an increase of 4 ml/kg/min in predicted aerobic capacity post-exercise training.

While there is observational evidence supporting the benefit of physical activity as protective for age-related cognitive decline (Quigley, MacKay-Lyons, et al., 2020), our pilot study did not show any effect of a structured, supervised, short-term exercise intervention on improving cognition. Concordant with our findings, a recent pilot RCT (Quigley, Brouillette, et al., 2020; $N = 22$) compared the potential benefit of a 3-month yoga training versus usual care and reported no within-group differences in B-CAM. Although between-group comparisons were made in

Table 2. Baseline characteristics of each of the three groups pre-exercise training.

Characteristic	Exercise group ($n = 27$) Mean (SD) or n (%)	Comparison group ($n = 114$) Mean (SD) or n (%)	Refusers ($n = 93$) Mean (SD) or n (%)
Age (years)	54.4 (6.5)	52.2 (8.2)	53.8 (8.1)
Sex			
Male	23 (85.0%)	89 (78.0%)	83 (89.0%)
Female	4 (15.0%)	25 (22.0%)	10 (11.0%)
Current daily activity			
Employed	7 (25.9%)	29 (25.4%)	39 (42.0%)
Unemployed	10 (37.0%)	2 (1.7%)	13 (14.0%)
Disability/ Retired/Other	10 (37.0%)	81 (72.8%)	41 (44.0%)
Years since HIV diagnosis	19.3 (7.0)	17.1 (8.1)	18.2 (7.2)
Smoking			
Yes	5 (18.5%)	37 (33.0%)	28 (30.43%)
No	21 (80.7%)	75 (67.0%)	60 (65.22%)
Body Mass Index (kg/m^2)	25.6	26.8	25.7

this study, it was not powered to do so. An earlier RCT (Fillipas et al., 2006; $N = 40$) compared 6-month, supervised, aerobic and resistance training to unsupervised walking and reported a between-group difference of 14 points (95% CI: 0.7–27.3) on the Cognitive subscale of MOS HIV. However, the controls scored 21% higher than the intervention group at baseline. Also, cognition was not the primary outcome in this study.

No clear exercise prescription guidelines exist for improving cognition in HIV (Quigley et al., 2019). However, some evidence has emerged in the aging literature. A recently undertaken systematic review of 98 clinical trials found that the median intervention time for studies with consistently positive outcomes was 52 h in older adults with and without cognitive impairment (Gomes-Osman et al., 2018). Among older adults with cognitive impairments, a meta-analysis ($N = 13$) revealed that exercise programs with a short session duration (<30 min) and high frequency (≥4 weeks) predicted higher effect sizes [0.43 (95% CI: 0.24–0.62)] and [0.50 (95% CI: 0.24–0.76)], respectively on cognitive outcomes (Sanders et al., 2019). Future studies in HIV should consider this evidence when designing exercise programs targeting cognition.

Table 3. Change in B-CAM pre-and post-exercise training in each of the study groups.

Outcome	Exercise group ($n = 27$) Mean (SD) / n (%)	Comparison group ($n = 114$) Mean (SD) / n (%)	Refusers ($n = 93$) Mean (SD) / n (%)
B-CAM (0–36)[a]			
Pre-exercise	20.4 (4.3)	16.1 (3.5)	17.0 (3.1)
Post-exercise	20.6 (4.5)	17.1 (3.7)	18.3 (3.4)
Change	0.2 (3.3)	0.9 (3.2)	1.3 (2.8)
Extent of change n (%)[b]			
Improvement: Change > 2.35	7 (26%)	33 (29%)	25 (27%)
Stable: Change −2.35 to +2.35	14 (52%)	67 (59%)	58 (62%)
Decline: Change < −2.35	6 (22%)	14 (12%)	10 (11%)
Reliable change: n (%)			
Positive[c]	1 (3.7%)	11 (10%)	7 (8%)
Negative	1 (3.7%)	3 (2.6%)	0

[a]Brief Cognitive Ability Measure; higher scores are better.
[b]Based on 1/2 SD for B-CAM.
[c]Greater than 1.645.

Table 4. Change in verbal fluency, comfortable and dual-task gait speed in the exercise group ($n = 27$).

Outcome	Mean (SD) or n (%)
Number of animals in a minute	
Pre-exercise [Norm 17 words]	19.3 (5.1)
Post-exercise	22.7 (5.3)
Change of MIC: n (%)[a]	4 (15.0%)
Reliable change: n (%)	1 (3.7%)
Comfortable gait speed	
Pre-exercise	1.2 (0.3)
Post-exercise	1.5 (0.2)
Change of MIC: n (%)	15 (55.5%)
Reliable change: n (%)	8 (30.0%)
Dual task gait speed	
Pre-exercise	1.1 (0.2)
Post-exercise	1.3 (0.4)
Change of MIC: n (%)	14 (52.0%)
Reliable change: n (%)	3 (11.1%)

[a]Minimal important change.

Table 5. Physical performance pre-and post-12 weeks of exercise program ($n = 27$).

Outcome	Pre-exercise Mean (SD)	Post-exercise Mean (SD)	Standardized response mean (SRM)	95% CI
Partial curl-ups (#)	8.9 (5.6)	18.0 (5.1)	1.5	1.12 to 2.25
Predicted VO_2max (ml/kg/min)	34.4(6.9)	38.4 (6.3)	0.9	0.61 to 1.37
Fast gait speed (m/s)	1.8 (0.3)	2.2 (0.4)	0.8	0.54 to 1.19
Seated leg extensor power (W)	204.0 (83.9)	240.3 (88.2)	0.8	0.41 to 1.19
Push-ups (#)	7.3 (5.2)	13.3 (6.3)	0.6	0.09 to 2.71
Six Minute Walk Test (m)	613.7 (83.9)	632.8 (55.2)	0.6	0.18 to 1.10
Averaged right grip strength (kg)	37.2 (7.8)	37.9 (8.2)	0.5	0.02 to 0.92
Averaged left grip strength (kg)	34.3 (8.5)	36.1 (9.3)	0.4	0.10 to 0.90
Jump height (cm)	32.0 (16)	32.7 (17)	0.2	−0.17 to 0.68

Table 6. Performance in brain health measures post-training in all the three groups.

Outcome	Exercise group ($n = 27$)		Comparison group ($n = 114$)		Refusers ($n = 93$)	
	Pre-Exercise Mean (SD)	Post- Exercise Mean (SD)	Pre-Exercise Mean (SD)	Post- Exercise Mean (SD)	Pre-Exercise Mean (SD)	Post- Exercise Mean (SD)
PDQ (0–80)[a]	35.3 (18.8)	34.7 (18.0)	43.9 (18.5)	42.9 (17.3)	36.0 (16.8)	34.5 (17.0)
MHI (0–100)[b]	60 (28–76)[e]	64 (44–80)	60 (48–80)	64 (48–80)	64 (48–78)	68 (48–80)
Vitality (0–100)[c]	55 (47–77)[f]	50 (35–75)	40 (35–60)	50 (30–65)	50 (35–70)	55 (40–70)
Motivation (0–42)[d]	27 (12.0)	29 (11.4)	26.3 (11.9)	25.8 (11.9)	25 (11.8)	25 (11.1)

[a] Perceived Deficits Questionnaire; a score of 40 or more is considered to indicate cognitive impairment.
[b]RAND-36 Mental Health Inventory; higher scores are better.
[c]RAND-36 Vitality Subscale; higher scores are better.
[d]Motivation (3 items); higher scores are better.
[e]Median (IQR) presented.
[f]Median (IQR) presented.

While we present both clinically meaningful change and reliable change for cognitive outcomes, we based our conclusions on reliable change. This is because MIC is based on an arbitrary cut-point while reliable change is based on the observed difference and correlation between pre-and post-values (Estrada et al., 2019). There were no important differences in the proportion making a reliable change in the study groups. Among exercisers, improvements in dual-task gait speed were promising as 11.1% showed reliable change. It is possible that exercising in a novel gym environment where new procedures (e.g., HIIT using elliptical machines, counting the sets and repetitions while lifting the weights) were involved and were potentially cognitively stimulating. A previous meta-analysis of the effect of exercise in HIV has reported clinically important changes in the MHI-5 [weighted mean difference (WMD) = 11.58; 95% CI: 1.35–21.81] and Vitality subscale of SF-36 (WMD = 5.03; 95% CI:1.33–8.72) (n = 59; O'Brien et al., 2016). On the contrary, our study did not find improvements in the brain health outcomes of anxiety/depression and fatigue probably due to the nature of the platform. The exercisers did not improve on the vertical jump test unlike other physical performance measures.

In terms of feasibility, there was good adherence to the intervention schedule and no adverse events were observed assuring it was a safe program for medically stable HIV+ adults. However, recruitment was sluggish. The most common reason for refusing participation was a lack of interest in exercise and unwillingness to commit to the time demand. A full-scale trial may not be feasible because there was almost no reliable change in cognition among the exercisers.

Strengths and limitations

While there were two comparison cohorts, there was no randomly assigned control group in this study. The intervention was supervised by a physiotherapist and a kinesiology student who ensured the intervention protocol was followed. They corrected the body mechanics and progressed the participants when appropriate. This type of professionally supervised exercise was chosen to maximize adherence to ensure that exercise components were sufficiently potent to affect changes in the exercise-induced mechanisms thought to influence cognition.

B-CAM has been developed using modern psychometric approach and is more feasible than the traditional methods involving resource-intensive, formal neuropsychological testing yielding a HAND classification of impaired or not impaired. B-CAM comprises standard neuropsychological tests chosen to have minimal practice effects and optimized for computer administration and statistical scoring (Brouillette et al., 2019).

The median duration between the intervention and the B-CAM evaluation was 28.0 days (IQR: 49.0). Cognition and other brain health measures take time to change. Using the CNS HIV Anti-Retroviral Therapy Effect Research (CHARTER) dataset, Brouillette et al. (2016) showed more than 80% of the HIV+ participants without any cognitive intervention remained stable in their cognition over 36 months using the group-based trajectory method. Having a scheduled evaluation time also provides real-world data to support the effect or lack thereof.

Conclusion

This feasibility study showed good adherence to the training schedule and acceptability of the 12-week intervention among people with HIV. Despite improvements in most of the outcomes of physical performance, there were no gains on cognitive performance. A future definitive trial may not be feasible with a similar design as exercise-induced benefits in physical performance did not yield cognitive benefits in this study. Further research is required to establish if there is an optimal exercise dose for improving cognition in HIV.

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References

American Thoracic Society. (2002). American Thoracic Statement: Guidelines for the six-minute walk test. *American Journal of Respiratory and Critical Care Medicine*, *166*(1), 111–117. doi:10.1164/ajrccm.166.1.at1102.

Bassey, E., & Short, A. (1990). A new method for measuring power output in a single leg extension: Feasibility, reliability and validity. *European Journal of Applied Physiology and Occupational Physiology*, *60*(5), 385–390. https://doi.org/10.1007/BF00713504

Billat, L. (2001). Interval training for performance: A scientific and empirical practice. *Sports Medicine*, *31*(2), 75–90. https://doi.org/10.2165/00007256-200131020-00001

Brouillette, M. J., Fellows, L. K., Finch, L., Thomas, R., & Mayo, N. E. (2019). Properties of a brief assessment tool for longitudinal measurement of cognition in people living with HIV. *Plos One*, *14*(3), e0213908. https://doi.org/10.1371/journal.pone.0213908

Brouillette, M. J., Fellows, L. K., Palladini, L., Finch, L., Thomas, R., & Mayo, N. E. (2015). Quantifying cognition at the bedside: A novel approach combining cognitive symptoms and signs in HIV. *BMC Neurology*, *15*(1), 224. https://doi.org/10.1186/s12883-015-0483-1

Brouillette, M. J., Yuen, T., Fellows, L. K., Cysique, L. A., Heaton, R. K., & Mayo, N. E. (2016). Identifying neurocognitive decline at 36 months among HIV-positive participants in the charter cohort using group-based trajectory analysis. *Plos One*, *11*(5), e0155766. https://doi.org/10.1371/journal.pone.0155766

Chaparro, C. G. A. P., Zech, P., Schuch, F., Wolfarth, B., Rapp, M., & Heiβel, A. (2018). Effects of aerobic and resistance exercise alone or combined on strength and hormone outcomes for people living with HIV. A meta-analysis. *PloS one*, *13*(9), e0203384. doi:10.1371/journal.pone.0203384.

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

Eldridge, S., Chan, C., Campbell, M., Bond, C., Hopewell, S., Thabane, L., Lancaster, G. A., & PAFS Consensus Group. (2016). Consort 2010 statement: Extension to randomised pilot and feasibility trials. *BMJ*, *355*, i5239. https://doi.org/10.1136/bmj.i5239

Estrada, E., Ferrer, E., & Pardo, A. (2019). Statistics for evaluating pre-post change: Relation between change in the distribution center and change in the individual scores. *Frontiers in Psychology*, *9*, 2696–2696. https://doi.org/10.3389/fpsyg.2018.02696

Fazeli, P. L., Marquine, M. J., Dufour, C., Henry, B. L., Montoya, J., Gouaux, B., Moore, R. C., Letendre, S. L., Woods, S. P., Grant, I., Jeste, D. V., Moore, D. J., & 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. https://doi.org/10.1007/s10461-015-1024-z

Fillipas, S., Oldmeadow, L., Bailey, M., & Cherry, C. (2006). A six-month, supervised, aerobic and resistance exercise program improves self-efficacy in people with human immunodeficiency virus: A randomised controlled trial. *Australian Journal of Physiotherapy*, *52*(3), 185–190. https://doi.org/10.1016/S0004-9514(06)70027-7

Gomes-Neto, M., Conceição, C., Oliveira, C., & Brites, C. (2015). Effects of combined aerobic and resistance exercise on exercise capacity, muscle strength and quality of life in HIV-infected patients: A systematic review and meta-analysis. *Plos One*, *10*(9), e0138066. https://doi.org/10.1371/journal.pone.0138066

Gomes-Osman, J., Cabral, D. F., Morris, T. P., McInerney, K., Cahalin, L. P., Rundek, T., Oliveira, A., & Pascual-Leone, A. (2018). Exercise for cognitive brain health in aging. *Neurology: Clinical Practice*, *8*(3), 257–265. https://doi.org/10.1212/CPJ.0000000000000460

Gueler, A., Moser, A., Calmy, A., Günthard, H. F., Bernasconi, E., Furrer, H., Fux, C. A., Battegay, M., Cavassini, M., Vernazza, P., Zwahlen, M., & Egger, M. for the Swiss HIV Cohort Study, Swiss National Cohort, Swiss National Cohort (2017). Life expectancy in HIV-positive persons in Switzerland. *Aids (London, England)*, *31*(3), 427–436. https://doi.org/10.1097/QAD.0000000000001335

Hays, R. D., Sherbourne, C. D., & Mazel, R. M. (1993). The RAND 36-item health survey 1.0. *Health Economics*, *2*(3), 217–227. https://doi.org/10.1002/hec.4730020305

Kelly, M., Loughrey, D., Lawlor, B., Robertson, I., Brennan, S., & Walsh, C. (2014). The impact of exercise on the cognitive functioning of healthy older adults: A systematic review and meta-analysis. *Ageing Research Reviews*, *16*(1), 12–31. https://doi.org/10.1016/j.arr.2014.05.002

Kern-Sanchez, N., & McGough, E. (2013). Physical exercise and cognitive performance in the elderly: Current perspectives. *Clinical Interventions in Aging*, *9*, 51–62. https://doi.org/10.2147/CIA.S39506

Malita, F. M., Karelis, A. D., Toma, E., & Rabasa-Lhoret, R. (2005). Effects of different types of exercise on body composition and fat distribution in HIV-infected patients: A brief review. *Canadian Journal of Applied Physiology*, *30*(2), 233–245. http://www.ncbi.nlm.nih.gov/pubmed/15981790 https://doi.org/10.1139/h05-117

Mayo, N. E., Brouillette, M. J., & Fellows, L. K., & Positive Brain Health Now Investigators. (2016). Understanding and optimizing brain health in HIV now: Protocol for a longitudinal cohort study with multiple randomized controlled trials. *BMC Neurology*, *16*. doi:10.1186/s12883-016-0527-1.

Norman, G., Sloan, J., & Wyrwich, K. (2004). The truly remarkable universality of half a standard deviation:

Confirmation through another look. *Expert Review of Pharmacoeconomics & Outcomes Research*, *4*(5), 581–585. https://doi.org/10.1586/14737167.4.5.581

O'Brien, K., Tynan, A., Nixon, S., & Glazier, R. (2016). Effectiveness of aerobic exercise for adults living with HIV: Systematic review and meta-analysis using the Cochrane Collaboration protocol. *BMC Infectious Diseases*, *16*(1), 182–182. https://doi.org/10.1186/s12879-016-1478-2

O'Brien, K., Tynan, A., Nixon, S., & Glazier, R. (2017). Effectiveness of progressive resistive exercise (PRE) in the context of HIV: Systematic review and meta-analysis using the Cochrane Collaboration protocol. *BMC Infectious Diseases*, *17*(1), 268–268. https://doi.org/10.1186/s12879-017-2342-8

Öhman, H., Savikko, N., Strandberg, T., & Pitkälä, K. (2014). Effect of physical exercise on cognitive performance in older adults with mild cognitive impairment or dementia: Asystematic review. *Dementia and Geriatric Cognitive Disorders*, *38*(5-6), 347–365. https://doi.org/10.1159/000365388

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 the International Neuropsychological Society*, *21*(10), 880–889. https://doi.org/10.1017/S1355617715000879

Plummer, P., & Iyigün, G. (2018). Effects of physical exercise interventions on dual-task gait speed following stroke: A systematic review and meta-analysis. *Archives of Physical Medicine and Rehabilitation*, *99*(12), 2548–2560. https://doi.org/10.1016/j.apmr.2018.04.009

Quigley, A., Brouillette, M. J., Gahagan, J., O'Brien, K. K., & MacKay-Lyons, M. (2020). Feasibility and impact of a yoga intervention on cognition, physical function, physical activity, and affective outcomes among people living with HIV: A randomized controlled pilot trial. *Journal of the International Association of Providers of AIDS Care (JIAPAC)*, *19*. https://doi.org/10.1177/2325958220935698

Quigley, A., MacKay-Lyons, M., & Eskes, G. (2020). Effects of exercise on cognitive performance in older adults: A narrative review of the evidence, possible biological mechanisms, and recommendations for exercise prescription. *Journal of Aging Research*, *2020*, 1–15. https://doi.org/10.1155/2020/1407896

Quigley, A., O'Brien, K., Parker, R., & MacKay-Lyons, M. (2019). Exercise and cognitive function in people living with HIV: A scoping review. *Disability and Rehabilitation*, *41*(12), 1384–1395. https://doi.org/10.1080/09638288.2018.1432079

Relton, C., Torgerson, D., O'Cathain, A., & Nicholl, J. (2010). Rethinking pragmatic randomised controlled trials: Introducing the "cohort multiple randomised controlled trial" design. *BMJ*, *340*(mar19_1), c1066. https://doi.org/10.1136/bmj.c1066

Sanders, L., Hortobágyi, T., la Bastide-van Gemert, S., van der Zee, E. A., & van Heuvelen, M. (2019). Dose-response relationship between exercise and cognitive function in older adults with and without cognitive impairment: A systematic review and meta-analysis. *PLOS One*, *14*(1), e0210036. https://doi.org/10.1371/journal.pone.0210036

Shao, Z., Janse, E., Visser, K., & Meyer, A. (2014). What do verbal fluency tasks measure? Predictors of verbal fluency performance in older adults. *Frontiers in Psychology*, *5*. https://doi.org/10.3389/fpsyg.2014.00772

Sullivan, M. J., Edgley, K., & Dehoux, E. (1990). A survey of multiple sclerosis: I. Perceived cognitive problems and compensatory strategy use. *Canadian Journal of Rehabilitation*, *4*, 99–105.

Terwee, C., Dekker, F., Wiersinga, W., Prummel, M., & Bossuyt, P. (2003). On assessing responsiveness of health-related quality of life instruments: Guidelines for instrument evaluation. *Quality of Life Research*, *12*(4), 349–362. https://doi.org/10.1023/A:1023499322593

Thomas, S., Reading, J., & Shephard, R. J. (1992). Revision of the Physical Activity Readiness Questionnaire (PAR-Q). *Canadian Journal of Sport Science*, *17*(4), 338–345.

Weller, I., Thomas, S., Corey, P., & Cox, M. (1993). Prediction of maximal oxygen uptake from a modified Canadian Aerobic Fitness Test. *Canadian Journal of Applied Physiology*, *18*(2), 175–188. https://doi.org/10.1139/h93-014

Williams, N. (2017). The Borg Rating of Perceived Exertion (RPE) scale. *Occupational Medicine*, *67*(5), 404–405. https://doi.org/10.1093/occmed/kqx063