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The acceptability and potential utility of cognitive training to improve working memory in persons living with HIV: A preliminary randomized trial

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Abstract

HIV-associated neurocognitive impairments that impact daily function persist in the era of effective antiretroviral therapy. Cognitive training, a promising low-cost intervention, has been shown to improve neurocognitive functioning in some clinical populations. We tested the feasibility, acceptability, and preliminary effects of computerized cognitive training to improve working memory in persons living with HIV infection (PLWH) and working memory impairment. In this randomized clinical trial, we assigned 21 adult PLWH to either an experimental cognitive training intervention or an attention-matched control training intervention. Participants completed 12 training sessions across 10 weeks with assessments at baseline and post-training. Session attendance was excellent and participants rated the program positively. Participants in the experimental arm demonstrated improved working memory function over time; participants in the control arm showed no change. Our results suggest that cognitive training may be a promising intervention for working memory impairment in PLWH and should be evaluated further.

Keywords

cognitive training; HIV; HIV-associated neurocognitive disorders; neuropsychology; working memory

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While the presentation of HIV-associated neurocognitive impairment (NCI) has evolved in the era of modern antiretroviral therapy (ART), HIV-associated NCI continues to be a serious complication of HIV infection (Heaton et al., 2010; Robertson et al., 2007; Sacktor, 2002). More than half of the 1.2 million persons living with HIV (PLWH) in the United States experience NCI (Centers for Disease Control and Prevention, 2015; Heaton et al., 2010). These impairments impact daily functioning and are predictive of adverse outcomes (Benedict, Mezhir, Walsh, & Hewitt, 2000; Gongvatana et al., 2009; Heaton, Marcotte, et al., 2004; Lovejoy & Suhr, 2009; Marcotte et al., 2004; Rabkin, McElhiney, Ferrando, Van Gorp, & Lin, 2004; Vivithanaporn et al., 2010). Of particular relevance for PLWH, NCI is associated with both increased HIV risk behaviors and suboptimal ART medication adherence, which in turn can exacerbate NCI (Anand, Springer, Copenhaver, & Altice, 2010; Shrestha & Copenhaver, 2016). The clinical focus for managing NCI thus far has been on optimizing medication regimens to minimize the impact of HIV on the central nervous system (Clifford & Ances, 2013), but more attention is needed on developing interventions that directly address the NCI that continues to occur despite ART.

In particular, working memory is an important target for intervention. Working memory involves short-term storage and processing of information from the present environment to accomplish complex cognitive tasks, which can include both reasoning and decision making (Baddeley, 1986). As a critical executive function, working memory has been linked closely to impulsive decision making (Hinson, Jameson, & Whitney, 2003; Shamosh et al., 2008) and self-regulation processes (Hofmann, Schmeichel, & Baddeley, 2012). Indeed, computerized working memory training led to decreased impulsive decision making in stimulant users in one study (Bickel, Yi, Landes, Hill, & Baxter, 2011). Working memory is particularly important for daily functioning, and research in PLWH has shown that working memory impairment is a strong predictor of failures in instrumental activities of daily living and other functional assessments (Heaton, Marcotte, et al., 2004).

Originally developed to treat the major cognitive deficits seen in schizophrenia, cognitive training has been successfully used in a range of conditions associated with cognitive deficits (e.g., aging, depression; Keshavan, Vinogradov, Rumsey, Sherrill, & Wagner, 2014). While some pilot work has been done (Becker et al., 2012; Boivin et al., 2010; Cody, Fazeli, & Vance, 2015; Vance, Fazeli, Ross, Wadley, & Ball, 2012), the potential for cognitive training to mitigate deficits found in HIV-associated NCI remains understudied. Cognitive training is a promising low-cost intervention that harnesses the brain’s neuroplastic capabilities. Training can be delivered by a therapist, workbook, or computer program, and progression is individualized as needed. Mechanistically, cognitive training is thought to target underlying neural processes using a variety of methods, including exercises to improve cognitive skills and compensatory strategies to minimize deficits (McGurk, Twamley, Sitzer, McHugo, & Mueser, 2007). Given potentially limited resources in clinical settings, cognitive training delivered via a computer program is particularly promising, as it would be low cost-effective and require minimal staff time.

We tested the feasibility and preliminary effects of a computerized cognitive training program to improve working memory in PLWH. In this randomized clinical trial, we assigned adult PLWH to one of two arms: the experimental intervention (active cognitive

training) or an attention control training intervention. Participants completed assessments at baseline and post-training. We hypothesized that participants assigned to active cognitive training, compared to those in the attention-matched control arm, would have greater improvements in working memory.

Methods

Procedures

Adult PLWH with working memory impairment were recruited from the Durham area between January 2015 and May 2016 via flyers and brochures at community-based organizations and infectious diseases clinics. Interested participants completed a brief preliminary eligibility screener and, if eligible, then completed an in-person visit that screened for study eligibility more comprehensively. Eligible participants returned for baseline assessment on another day.

The baseline assessment included a neuropsychological battery to assess current functioning. After completing the baseline assessment, participants were randomly assigned to one of two arms (active cognitive training or control training) using simple randomization generated by a computer program. Randomization was completed by the principal investigator after baseline assessment so that assignment was unknown at the time of baseline evaluation. The study team was not blinded to treatment assignment after randomization. Participants in both arms then completed 12 training sessions, which occurred over 10 weeks. The first session was scheduled within 1 week of the baseline. Participants were asked to schedule 2 sessions per week, but 10 weeks were allowed to account for missed or cancelled sessions. Participants were not allowed to exceed 2 sessions per week. At training sessions, participants assigned to the active cognitive training group completed computerized modules designed to enhance working memory, while those assigned to the attention-matched control group completed inactive modules that were not designed to enhance memory. Training sessions consisted of 5 commercially available memory-training tasks from the PSSCogRehab software program, which has been used in a wide variety of conditions including schizophrenia, brain injury, and substance abuse (http://www.psychological-software.com/PSS/pssnew/). Within 1 week of the last session, participants returned to complete a post-training assessment to evaluate the effects of the training intervention.

Participants were compensated for all visits, including sessions. They received $35 USD for the screening visit, $65 USD for the baseline visit, and $85 USD for the post-training follow-up. For training sessions, participants were compensated $10 USD for each attended session for their time, and earned a cumulative $1 USD bonus for each consecutively attended session to encourage consistent session attendance. Therefore, participants could earn up to $21 USD for the final session if all 12 sessions were completed consecutively within the 10-week time frame. Total potential earnings for completing all sessions were $186 USD. To maintain the attendance bonus, participants were required to attend at least one session per week. The bonus reset to $1 USD if the participant failed to attend at least 1 session per week.

Figure 1 shows the flow of participants through the study. Study procedures were approved by the institutional review board at Duke University Health System and was registered on ClinicalTrials.gov (Identifier: NCT02216591). Participants provided written informed consent prior to any study activities.

Eligibility Criteria

The sample included adults living with HIV infection, ages 18–65 years, and living independently in the community; the study was open to all gender and racial/ethnic identities. Participants had to be in HIV care and on ART for more than 3 months. Because the intervention target was working memory, participants had to demonstrate working memory impairment, defined as either (a) a T score less than or equal to 40 (i.e., more than one standard deviation below average performance) on at least 1 of 2 tests of working memory, or (b) T scores less than or equal to 50 (the normative mean) on both tests of working memory. Exclusion criteria included a diagnosis of current substance use disorder and/or any drug use other than alcohol or marijuana in the previous 90 days (as verified by interview and a urine drug screen). To minimize potential confounds, individuals had to be diagnosed with HIV for longer than 6 months (i.e., no longer experiencing acute HIV infection). To minimize potential attrition, individuals who lived more than 15 miles away from Duke Medical Center and individuals who stated they were planning to move away from the area within the next 3 months were excluded. Additional exclusion criteria were: English non-fluency; 8th grade education or less; serious neurological disorders, including HIV dementia; traumatic brain injury; severe mental illness or acute psychiatric distress; impaired mental status; or pregnancy.

Screening Measures

The screening visit included clinical interviews of HIV tests and staging (RAND Corporation, 2007), HIV medication adherence (Giordano, Guzman, Clark, Charlebois, & Bangsberg, 2004), medical, psychiatric and substance use history (First, Spitzer, Gibbon, & Williams, 1996; McGahan, Griffith, Parente, & McLellan, 1986; McLellan et al., 1992; Sheehan et al., 1998), and computerized questionnaires that assessed demographics. The visit also included urine tests for pregnancy and recent drug use. Participants completed the Wechsler Test of Adult Reading, which estimated premorbid verbal IQ by asking participants to read aloud 50 words that had atypical grapheme to phoneme translations (Wechsler, 2001). To assess current working memory function, participants completed the NAB Digits Forward/Digits Backward Test (Stern & White, 2009). Finally, participants provided authorization for the release of their health care records to research staff, who abstracted HIV clinical variables, including the date of HIV diagnosis, most recent and nadir CD4+ T cell count, most recent HIV viral load test, and history of an AIDS diagnosis.

Neuropsychological Assessment

Neuropsychological function was assessed using a 45-minute battery that covered 7 domains of function. The domains were consistent with recommendations for assessing HIV-associated NCI, and similar batteries have been found to be sensitive to HIV-associated NCI (Antinori et al., 2007). While working memory was the primary outcome measure of interest, 6 additional domains were assessed to examine the specificity of the training:

1. *Processing speed:* Trail Making Test Part A – number of seconds to completion (Reitan & Wolfson, 1993)
2. *Learning (immediate recall):* Hopkins Verbal Learning Test – Revised (HVLT-R) – total number of words recalled on trials 1–3 (Brandt & Benedict, 2001)
3. *Memory (delayed recall):* HVLT-R – number of words recalled on trial 4 (Brandt & Benedict, 2001)
4. *Executive function:* Stroop Color and Word Test interference score – difference between actual and predicted score on the Color-Word trial (Golden, 1978); Trail Making Test Part B – number of seconds to completion (Reitan & Wolfson, 1993)
5. *Verbal fluency:* FAS letter fluency – number of words generated; and category fluency – number of animals generated (Benton, Hamsher, & Sivan, 1983)
6. *Working memory:* Paced Auditory Serial Addition Task-50 – number correct (Diehr et al., 2003); NAB Digits Forward/Digits Backward Test – number correct (Stern & White, 2009)
7. *Motor skills*: Grooved Pegboard Test dominant and non-dominant hand – number of seconds to completion (Klove, 1963)

Using the most up-to-date published normative data, raw test scores were converted to T-scores that corrected for demographic factors such as age and education (Diehr et al., 2003; Heaton, Miller, Taylor, & Grant, 2004; Norman et al., 2011; Stern & White, 2009). Overall domain scores were computed by averaging T-scores of the tests within each domain.

Intervention Arms

Active Cognitive Training (ACT)—Five modules from PSSCogRehab were used:

1. Sequenced recall of digits - auditory (SRD-A): Participants recalled numbers presented aloud. The first trial included three numbers, and each subsequent trial increased by one digit following a correct response. If the participant responded incorrectly, a different sequence of the same length was presented. The test ended after five misses.
2. Sequenced Recall Reversed Digits - Auditory (SRRD-A): This module had the same requirements as SRD-A, except that participants recalled the digits in the reverse order.
3. Sequenced Recall of Words - Visual (SRW-V): Participants studied a list of four-letter words and then attempted to find them in the correct order from a list of 16 words. The first trial included three words, and each subsequent trial increased by one word following a correct response, up to 11-words. If the participant responded incorrectly, a different list of the same number of words was presented. The test ended after five misses.
4. Spatial Memory – Objects and Locations (SM-OL). Participants viewed a display of 30 pictures. Some of the pictures then appeared on the screen for the

participants to memorize. All 30 pictures then re-appeared and participants selected the pictures they memorized. If the participant provided an incorrect response, the same array was repeated. The test ended after four misses.

5. Visual Memory – Sequenced Blocks (VM-SB). Participants saw 12 blocks on the screen and watched a hand-shaped cursor touch a series of them. Then participants selected the blocks in the same order. If a participant made an error, the same sequence was presented. The test ended after three errors in the same sequence.

In each training session, participants completed each of the memory training modules once and then completed the module a second time if the first administration did not last at least 5 minutes.

Control Training (CON)—The same computer modules were used in the control group sessions. However, the control modules did not progressively increase in difficulty across trials, such that participants' working memory was not challenged over the course of the modules. Participants in the CON group completed each module at the lowest level of difficulty for 5 minutes per module.

Follow-Up Procedures

The full neuropsychological assessment battery was repeated at the post-training follow-up visit. Participants also completed an intervention process assessment to describe their experiences of the intervention and provide feedback on perceived benefits; barriers to attendance; and the length, number, and content of sessions. The assessment included ratings of satisfaction and helpfulness. Participants used a 5-point scale to rate their overall satisfaction with the program (1 = *Very dissatisfied*, 2 = *Somewhat dissatisfied*, 3 = *Neutral*, 4 = *Somewhat satisfied*, 5 = *Very satisfied*) as well as how helpful they thought the program was (1 = *Very unhelpful*, 2 = *Somewhat unhelpful*, 3 = *Neutral*, 4 = *Somewhat helpful*, 5 = *Very helpful*).

Data Analysis

Analyses were conducted using SPSS 24.0.0.0. Descriptive statistics were used to characterize the sample, and baseline group differences on demographic and HIV characteristics were examined using chi-square, independent samples t-tests, and the Mann-Whitey U test. To examine feasibility and acceptability, independent samples t-tests were used to examine group differences on session attendance and intervention process assessment questionnaire responses. To examine intervention effects on neuropsychological outcomes, we conducted a series of 2 (Arm: ACT vs. CON) × 2 (Time: Baseline vs. Post) mixed-model general linear model analyses. Time was the within-subjects factor defined by baseline versus post-training follow-up, and study arm was the between-subjects factor. Age and years of education were included as covariates.

Results

Sample Characteristics

The sample included 21 adults. Eleven participants were randomized to the ACT arm and 10 participants were randomized to the CON arm. The sample was mostly male (n = 16, 76%) and African American (n = 18, 86%). Participants were 47.90 years of age on average (SD = 11.15), with a mean of 13.38 years of education (SD = 2.46), and most (82%) had at least a high school education. Participants had been diagnosed with HIV for 13.86 years on average (SD = 7.99). All participants were receiving ART and were prescribed an average of 2.05 HIV different pills (SD = 1.02). Participants reported taking approximately 93% (SD = 15%) of the prescribed doses of ART in the 4 weeks prior to the screening visit. Nearly half the sample (n = 10, 48%) had a detectable viral load (≥ 50 copies/mL). The median most recent CD4+ T cell count was 561 cells/mm^3 (IQR = 410) and the median nadir CD4+ T cell count was 135 cells/mm^3 (IQR = 348). Table 1 compares the study groups on demographic, HIV, and other characteristics. There were no group differences on any of these characteristics, indicating that randomization was effective.

Feasibility and Acceptability

Participants completed an average of 11.38 (SD = 2.25) sessions out of 12 possible. Within the ACT group, 100% (n = 11) of participants completed all sessions. Within the CON group, 80% (n = 8) of participants completed all sessions. Of the 2 CON participants who did not complete all sessions, one completed 9 sessions and the other completed only 2 sessions. Both participants reported that work schedules were the principal obstacle to completing more sessions.

There was no difference between arms on overall satisfaction and helpfulness ratings, with participants in both groups indicating that they felt satisfied with the sessions and found them helpful. As shown in Table 2, the ratings between groups were highly similar, with group differences occurring in only 2 items. ACT participants more strongly disagreed than CON participants with the statement that using the computer during sessions was difficult, and participants in the ACT group more strongly agreed that they would be willing to complete a similar program of training on their own than the CON participants.

Post-Intervention Outcomes

Retention to the post-training follow-up was high (95%), with 20 out of 21 participants completing the follow-up. The participant who did not complete the follow-up was the participant assigned to the CON arm who completed only 2 training sessions. We made extensive outreach attempts to schedule him for his post-training follow-up despite his drop-out from sessions, but he did not respond to outreach attempts. Therefore, the sample for outcome analyses included 11 participants from the ACT arm and 9 participants from the CON arm.

In the 2 (Arm) × 2 (Time) mixed-model general linear model on working memory with age and education covaried, a significant main effect of time, $F(1,16) = 6.89$, $p = 0.018$, was qualified by a significant interaction effect of time by arm, $F(1,16) = 7.76$, $p = 0.013$.

Adjusted means indicated that participants in ACT showed a significant increase in the mean working memory T score from baseline (M = 45.08) to post (M = 51.33) compared to CON participants (η^2= .327, indicating a large effect size), whose scores were largely unchanged (baseline M = 43.89 and post M = 43.15). There were no significant main or interaction effects for any other domains examined (all p > .05).

Discussion

Our study provides preliminary support for the acceptability and potential efficacy of a computerized cognitive training program to improve working memory function in a sample of PLWH with working memory impairment. Overall, participants were satisfied with the program and rated it positively. Outcome analyses supported that this type of computerized training could significantly improve working memory performance. Indeed, for participants in the ACT arm, working memory standardized T scores went from 5 points below mean performance to just over mean performance at the post-training follow-up, while performance in the CON group was unchanged.

The results support our hypothesis that the cognitive training program would lead to improvements in working memory for the active training group, and that working memory for the control training group would not change. We found no other significant effects across any of the other neuropsychological domains measured, which indicated that that the effects of training were specific to working memory function. These findings provide support for the potential of working memory training to be an effective intervention for HIV-associated working memory impairment. Our findings add to an emerging literature that supports the feasibility of computerized cognitive training and its potential efficacy in other cognitive domains for PLWH. One study in a cohort of children living with HIV infection in Uganda found that a computerized training program for simple attention and processing speed showed promising results in improving function in those domains (Boivin et al., 2010). Another study examined a cognitive stimulant program in a sample of 60 participants (with and without HIV infection) and found that neurocognitive function improved for participants who used the program the most (Becker et al., 2012). Two other studies using speed of processing training in middle-aged and older adults with HIV also showed promising effects of training on neurocognitive outcomes (Cody et al., 2015; Vance et al., 2012). Our study is the first to focus on working memory, a core cognitive function that is important for daily living.

Based on responses to the intervention process assessment, participants perceived the training program to be helpful. Participants across both arms rated the program highly across multiple characteristics and, most importantly, participants in the ACT group expressed willingness to complete a program such as this on their own. These results support the feasibility of implementing this type of intervention and indicate that it was acceptable to participants. Importantly, participants did not endorse attending solely because of the monetary reimbursement for sessions or the attendance bonuses. In addition to participant ratings, session attendance for enrolled participants was excellent, with all ACT participants completing 100% of sessions. High attendance rates also support the feasibility and acceptability of the intervention.

Recruitment was a significant challenge during this clinical trial, with an average enrollment of 1 per month. Recruitment was extended for 6 months in order to reach a final sample size of at least 20 participants. There were two major barriers to enrollment, both of which primarily occurred before an in-person appointment was ever scheduled. First, at pre-screening, many participants declined to participate after hearing about study details because coming to the lab twice per week during regular business hours to complete the sessions was impractical due to work or other commitments. Second, many patients were ruled out at pre-screening because they lived more than 15 miles away from the medical center. This eligibility criterion was intended to minimize attrition in the clinical trial, but it also excluded a proportion of the patients served at local HIV clinics who traveled a good distance for their appointments. Our medical center serves a large catchment area, including patients living in rural communities of North Carolina and surrounding states. With increasing recognition of the physical barriers to HIV care and associated treatments, the National HIV/AIDS Strategy for the United States has emphasized the importance of developing innovative models of care to improve access for those living in remote or rural areas (The White House, 2015). To address these challenges, future trials examining cognitive training should use web-based services that can be completed remotely, either at home or at a facility where computers are available for public use (e.g., a library).

Our study had several notable strengths, including a sound experimental design, comprehensive assessment battery, and excellent retention rates. Moreover, we observed a significant effect in working memory that supported the potential efficacy of the cognitive training program used in this study. At the same time, the study had several limitations that should be discussed. First, the duration and frequency of the intervention (12 sessions over about 6 weeks) was fairly minimal intensity compared to other cognitive training interventions (Vinogradov, Fisher, & de Villers-Sidani, 2012). Future studies should test whether effects can be enhanced by using more intensive interventions. Second, the post-training follow-up occurred within 1 week of the final training session, so our results do not speak to the long-term durability of training effects. Longer follow-up periods are necessary to assess how long functional gains made during training are maintained. Third, our sample demonstrated only moderate working memory impairment at baseline. Future studies should focus on vulnerable populations, including those with more serious working memory impairment or those with co-morbid conditions that might contribute to NCI, such as substance abuse. Finally, there was some overlap in the cognitive training tasks (sequenced recall of digits and sequenced recall of digits reversed) and the working memory assessment used at baseline and post-training (Digit Span forwards and backwards). Therefore, it is possible that participants improved on those tasks specifically as a result of training and those improvements may not generalize to all aspects of working memory function. Future studies should use training tasks and neuropsychological assessments that do not have this type of overlap. In addition, future studies should include assessments that evaluate real-world functional impairments associated with NCI.

Conclusions

In conclusion, we have demonstrated the feasibility, acceptability, and preliminary efficacy of computerized working memory training. Our results highlight that cognitive training is a

potentially useful intervention to address HIV-associated NCI. Additional research with larger sample sizes are needed to confirm the efficacy of this intervention and to evaluate Web-based cognitive training to improve dissemination to a larger number of PLWH who experience NCI.

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References

Anand P, Springer SA, Copenhaver MM, Altice FL. Neurocognitive impairment and HIV risk factors: A reciprocal relationship. AIDS and Behavior. 2010; 14(6):1213–1226. DOI: 10.1007/s10461-010-9684-1 [PubMed: 20232242]

Antinori A, Arendt G, Becker JT, Brew BJ, Byrd DA, Cherner M, … Wojna VE. Updated research nosology for HIV-associated neurocognitive disorders. Neurology. 2007; 69(18):1789–1799. DOI: 10.1212/01.WNL.0000287431.88658.8b [PubMed: 17914061]

Baddeley, AD. Working memory. Oxford, England: Oxford University Press; 1986.

Becker JT, Dew MA, Aizenstein HJ, Lopez OL, Morrow L, Saxton J, Tarraga L. A pilot study of the effects of Internet-based cognitive stimulation on neuropsychological function in HIV disease. Disability and Rehabilitation. 2012; 34(21):1848–1852. DOI: 10.3109/09638288.2012.667188 [PubMed: 22458375]

Benedict RHB, Mezhir JJ, Walsh K, Hewitt RG. Impact of human immunodeficiency virus type-1-associated cognitive dysfunction on activities of daily living and quality of life. Archives of Clinical Neuropsychology. 2000; 15(6):535–544. DOI: 10.1016/S0887-6177(99)00044-X [PubMed: 14590207]

Benton, A., Hamsher, K., Sivan, A. Multilingual Aphasia Examination. 3. Iowa City, IA: AJA Associates; 1983.

Bickel WK, Yi R, Landes RD, Hill PF, Baxter C. Remember the future: Working memory training decreases delay discounting among stimulant addicts. Biological Psychiatry. 2011; 69(3):260–265. DOI: 10.1016/j.biopsych.2010.08.017 [PubMed: 20965498]

Boivin MJ, Busman RA, Parikh SM, Bangirana P, Page CF, Opoka RO, Giordani B. A pilot study of the neuropsychological benefits of computerized cognitive rehabilitation in Ugandan children with HIV. Neuropsychology. 2010; 24(5):667–673. DOI: 10.1037/a0019312 [PubMed: 20804255]

Brandt, J., Benedict, RHB. Hopkins Verbal Learning Test -- Revised professional manual. Lutz, FL: Psychological Assessment Resources, Inc; 2001.

Centers for Disease Control and Prevention. Monitoring selected national HIV prevention and care objectives by using HIV surveillance data – United States and 6 dependent areas – 2013. 2015. Retrieved from http://www.cdc.gov/hiv/library/reports/surveillance/

Clifford DB, Ances BM. HIV-associated neurocognitive disorder. Lancet Infectious Diseases. 2013; 13(11):976–986. DOI: 10.1016/S1473-3099(13)70269-X [PubMed: 24156898]

Cody SL, Fazeli PL, Vance DE. Feasibility of a home-based speed of processing training program in middle-aged and older adults with HIV. Journal of Neuroscience Nursing. 2015; 47(4):247–254. DOI: 10.1097/jnn.0000000000000147 [PubMed: 26153789]

Diehr MC, Cherner M, Wolfson TJ, Miller SW, Grant I, Heaton RK. The 50 and 100-item short forms of the Paced Auditory Serial Addition Task (PASAT): Demographically corrected norms and comparisons with the full PASAT in normal and clinical samples. Journal of Clinical and Experimental Neuropsychology. 2003; 25(4):571–585. DOI: 10.1076/jcen.25.4.571.13876 [PubMed: 12911108]

First, MB., Spitzer, RL., Gibbon, M., Williams, JBW. Structured clinical interview for DSM-IV Axis I disorders, research version, patient/non-patient edition. New York, NY: Biometrics Research, New York State Psychiatric Institute; 1996.

Giordano TP, Guzman D, Clark R, Charlebois ED, Bangsberg DR. Measuring adherence to antiretroviral therapy in a diverse population using a visual analogue scale. HIV Clinical Trials. 2004; 5(2):74–79. DOI: 10.1310/JFXH-G3X2-EYM6-D6UG [PubMed: 15116282]

Golden, CJ. Stroop Color and Word Test. Chicago, IL: Stoelting; 1978.

Gongvatana A, Schweinsburg BC, Taylor MJ, Theilmann RJ, Letendre SL, Alhassoon OM, … Grant I. White matter tract injury and cognitive impairment in human immunodeficiency virus-infected individuals. Journal of Neurovirology. 2009; 15(2):187–195. DOI: 10.1080/13550280902769756 [PubMed: 19306228]

Heaton RK, Clifford DB, Franklin DR Jr, Woods SP, Ake C, Vaida F, … Grant I. HIV-associated neurocognitive disorders persist in the era of potent antiretroviral therapy: CHARTER Study. Neurology. 2010; 75(23):2087–2096. DOI: 10.1212/WNL.0b013e318200d727 [PubMed: 21135382]

Heaton RK, Marcotte TD, Mindt MR, Sadek J, Moore DJ, Bentley H, … Grant I. The impact of HIV-associated neuropsychological impairment on everyday functioning. Journal of the International Neuropsychological Society. 2004; 10(3):317–331. DOI: 10.1017/S1355617704102130 [PubMed: 15147590]

Heaton, RK., Miller, SW., Taylor, MJ., Grant, I. Revised comprehensive norms for an expanded Halstead-Reitan battery: Demographically adjusted neuropsychological norms for African American and Caucasian adults. Lutz, FL: Psychological Assessment Resources, Inc; 2004.

Hinson JM, Jameson TL, Whitney P. Impulsive decision making and working memory. Journal of Experimental Psychology: Learning, Memory, and Cognition. 2003; 29(2):298–306. DOI: 10.1037/0278-7393.29.2.298

Hofmann W, Schmeichel BJ, Baddeley AD. Executive functions and self-regulation. Trends in Cognitive Sciences. 2012; 16(3):174–180. DOI: 10.1016/j.tics.2012.01.006 [PubMed: 22336729]

Keshavan MS, Vinogradov S, Rumsey J, Sherrill J, Wagner A. Cognitive training in mental disorders: Update and future directions. American Journal of Psychiatry. 2014; 171(5):510–522. DOI: 10.1176/appi.ajp.2013.13081075 [PubMed: 24700194]

Klove, H. Grooved pegboard. Lafayette, IN: Lafayette Instruments; 1963.

Lovejoy TI, Suhr JA. The relationship between neuropsychological functioning and HAART adherence in HIV-positive adults: A systematic review. Journal of Behavioral Medicine. 2009; 32(5):389–405. DOI: 10.1007/s10865-009-9212-9 [PubMed: 19291386]

Marcotte TD, Wolfson T, Rosenthal TJ, Heaton RK, Gonzalez R, Ellis RJ, Grant I. A multimodal assessment of driving performance in HIV infection. Neurology. 2004; 63(8):1417–1422. DOI: 10.1212/01.WNL.0000141920.33580.5D [PubMed: 15505158]

McGahan, PL., Griffith, JA., Parente, R., McLellan, AT. Addiction Severity Index composite scores mannual. Philadelphia, PA: University of Pennsylvania/Veterans Administration Center for Studies of Addiction; 1986.

McGurk SR, Twamley EW, Sitzer DI, McHugo GJ, Mueser KT. A meta-analysis of cognitive remediation in schizophrenia. American Journal of Psychiatry. 2007; 164(12):1791–1802. DOI: 10.1176/appi.ajp.2007.07060906 [PubMed: 18056233]

McLellan AT, Kushner H, Metzger D, Peters R, Smith I, Grissom G, … Argeriou M. The fifth edition of the Addiction Severity Index. Journal of Substance Abuse Treatment. 1992; 9(3):199–213. DOI: 10.1016/0740-5472(92)90062-S [PubMed: 1334156]

Norman MA, Moore DJ, Taylor M, Franklin D Jr, Cysique L, Ake C, … Heaton RK. Demographically corrected norms for African Americans and Caucasians on the Hopkins Verbal Learning Test-Revised, Brief Visuospatial Memory Test-Revised, Stroop Color and Word Test, and Wisconsin Card Sorting Test 64-Card Version. Journal of Clinical and Experimental Neuropsychology. 2011; 33(7):793–804. DOI: 10.1080/13803395.2011.559157 [PubMed: 21547817]

Rabkin JG, McElhiney M, Ferrando SJ, Van Gorp W, Lin SH. Predictors of employment of men with HIV/AIDS: A longitudinal study. Psychosomatic Medicine. 2004; 66(1):72–78. DOI: 10.1097/01.PSY.0000108083.43147.6D [PubMed: 14747640]

RAND Corporation. HIV Cost and Services Utilization Study (HCSUS) baseline questionnaire. Santa Monica, CA: RAND Corporation; 2007.

Reitan, RM., Wolfson, D. The Halstead-Reitan neuropsychological test battery: Theory and clinical interpretation. 2. Tucson, AZ: Neuropsycholgy Press; 1993.

Robertson KR, Nakasujja N, Wong M, Musisi S, Katabira E, Parsons TD, … Sacktor N. Pattern of neuropsychological performance among HIV positive patients in Uganda. BMC Neurology. 2007; 7:8.doi: 10.1186/1471-2377-7-8 [PubMed: 17411437]

Sacktor N. The epidemiology of human immunodeficiency virus-associated neurological disease in the era of highly active antiretroviral therapy. Journal of Neurovirology. 2002; 8(Suppl 2):115–121. DOI: 10.1080/13550280290101094 [PubMed: 12491162]

Shamosh NA, DeYoung CG, Green AE, Reis DL, Johnson MR, Conway ARA, … Gray JR. Individual differences in delay discounting: Relation to intelligence, working memory, and anterior prefrontal cortex. Psychological Science. 2008; 19(9):904–911. DOI: 10.1111/j.1467-9280.2008.02175.x [PubMed: 18947356]

Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, … Dunbar GC. The Mini International Neuropsychiatric Interview (M.I.N.I.): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. Journal of Clinical Psychiatry. 1998; 59(Suppl 30):22–33.

Shrestha R, Copenhaver M. The influence of neurocognitive impairment on HIV risk behaviors and intervention outcomes among high-risk substance users: A systematic review. Frontiers In Public Health. 2016; 4:1–6. DOI: 10.3389/fpubh.2016.00016 [PubMed: 26870721]

Stern, RA., White, T. NAB Digits Forward/Digits Backward Test: Professional manual. Lutz, FL: Psychological Assessment Resources, Inc. (PAR); 2009.

The White House. National HIV/AIDS Strategy for the United States: Updated to 2020. 2015. Retrieved from http://www.aids.gov/federal-resources/national-hiv-aids-strategy/nhas-update.pdf

Vance DE, Fazeli PL, Ross LA, Wadley VG, Ball KK. Speed of processing training with middle-age and older adults with HIV: A pilot study. Journal of the Association of Nurses in AIDS Care. 2012; 23(6):500–510. DOI: 10.1016/j.jana.2012.01.005 [PubMed: 22579081]

Vinogradov S, Fisher M, de Villers-Sidani E. Cognitive training for impaired neural systems in neuropsychiatric illness. Neuropsychopharmacology. 2012; 37(1):43–76. DOI: 10.1038/npp.2011.251 [PubMed: 22048465]

Vivithanaporn P, Heo G, Gamble J, Krentz HB, Hoke A, Gill MJ, Power C. Neurologic disease burden in treated HIV/AIDS predicts survival: A population-based study. Neurology. 2010; 75(13):1150–1158. DOI: 10.1212/WNL.0b013e3181f4d5bb [PubMed: 20739646]

Wechsler, D. Wechsler Test of Adult Reading (WTAR) manual. San Antonio, TX: Harcourt Assessment; 2001.

Key Considerations

- Working memory impairment, a common feature of HIV-associated neurocognitive disorder, can have impact on other aspects of cognition as well as on daily function.
- Developing cost-effective interventions to address this impairment in persons living with HIV is critical.
- Computerized cognitive training is a particularly promising intervention, as it is low-cost and requires minimal staff time.
- The results of our pilot study demonstrated the feasibility, acceptability, and preliminary efficacy of computerized working memory training to address working memory impairment in persons living with HIV infection.
- Additional research with larger sample sizes are needed to confirm the efficacy of this intervention.

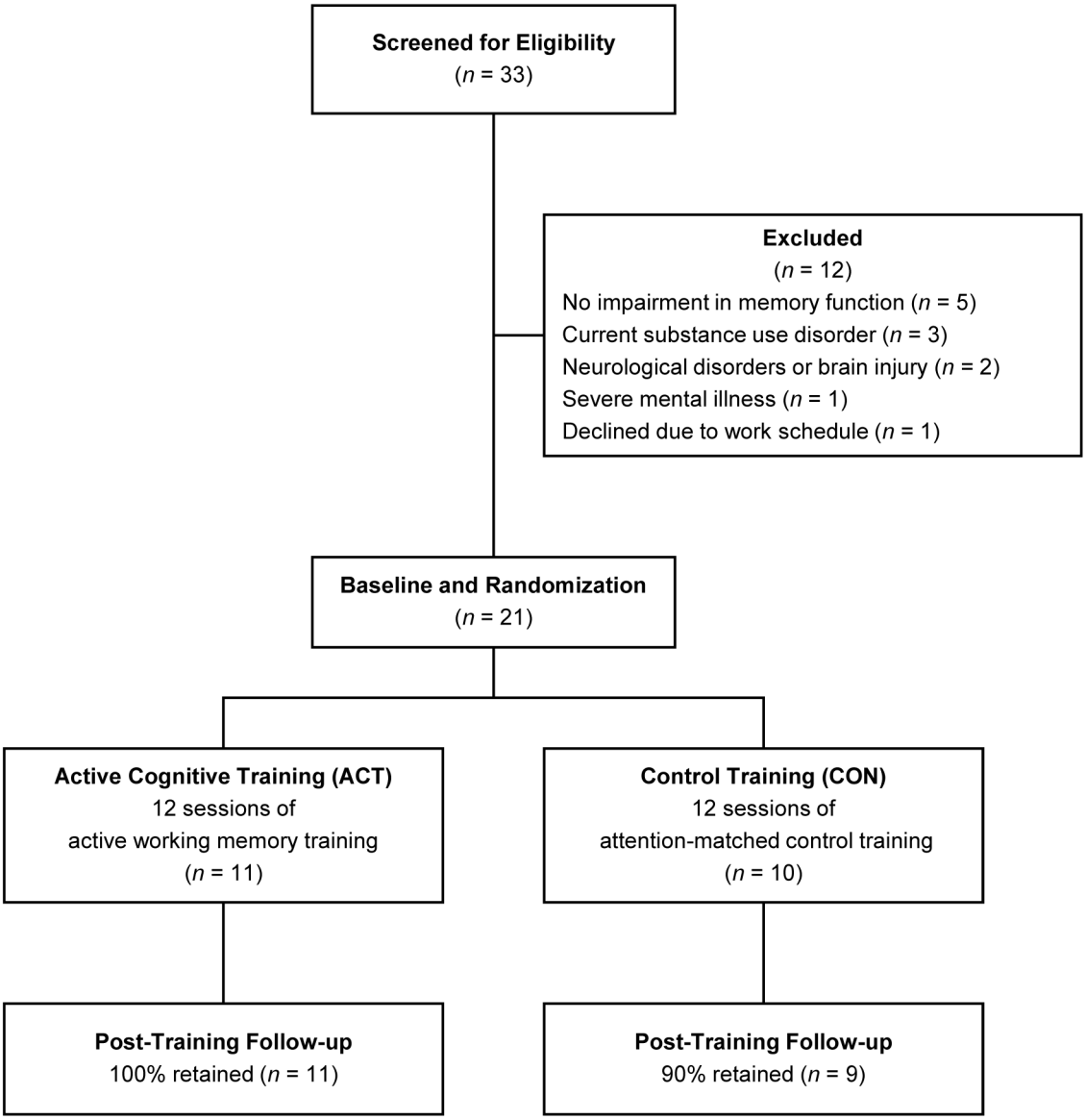

Figure 1.
Flow diagram of participant recruitment, enrollment and retention.

Table 1

Participant Characteristics of the Two Study Groups ($N = 21$)

	ACT ($n = 11$)	CON ($n = 10$)	Statistic
Demographic and other characteristics			
Female, *n* (%)	3 (27%)	2 (20%)	$\chi^2(1) = 0.15$
Age in years, *M* (*SD*)	51.27 (8.37)	44.20 (13.01)	$t(19) = 1.50$
Race, *n* (%)			$\chi^2(12) = 0.51$
African American	10 (91%)	8 (80%)	
Caucasian	1 (9%)	2 (20%)	
Education in years, *M* (*SD*)	14.09 (2.88)	12.60 (1.71)	$t(19) = 1.42$
Premorbid verbal IQ, *M* (*SD*)	96.45 (19.41)	90.10 (20.31)	$t(19) = 0.73$
Number of sessions attended, *M* (*SD*)	12.00 (0.00)	10.70 (3.20)	$t(19) = 1.35$
HIV characteristics			
Years since HIV diagnosis, *M* (*SD*)	13.91 (7.26)	13.80 (9.13)	$t(36) = 0.30$
Nadir CD4+ T cells/mm^3, *Mdn* (*IQR*)	200 (394)	82 (305)[a]	$U = 43.00$
Current CD4+ T cells/mm^3, *Mdn* (*IQR*)	711 (695)	474 (378)[a]	$U = 34.00$
Detectable HIV viral load, *n* (%)	6 (55%)	4 (40%)	$\chi^2(1) = 0.44$
AIDS diagnosis, *n* (%)	5 (46%)	5 (56%)[a]	$\chi^2(1) = 0.20$

Note. M = Mean; SD = Standard deviation; Mdn = Median; IQR = interquartile range; all $p < 0.05$;

[a]CON $n = 9$ and % out of 9 due to missing data for one participant;

ACT = Active Cognitive Training; CON = Control Training.

Table 2

Means and Standard Deviations of Participant Ratings of the Intervention ($N = 20$)

	ACT ($n = 11$)	CON ($n = 9$)[a]	Statistic (t-test)
Perceptions of the training program			
The training sessions were interesting	4.55 (0.52)	4.00 (0.87)	$t(18) = 1.74$
I enjoyed the training sessions	4.27 (0.90)	4.33 (0.71)	$t(18) = 0.16$
Using the computer during the sessions was difficult	1.09 (0.30)	2.00 (1.32)	$t(18) = 2.22^*$
I liked the computer program used in the training sessions	4.55 (0.52)	4.33 (0.87)	$t(18) = 0.68$
I would be willing to complete a program like this on my own, either on a personal computer or mobile device	4.45 (0.52)	3.89 (0.60)	$t(18) = 2.25^*$
Factors affecting attendance			
I attended training sessions because I thought they would be helpful to me	4.45 (0.69)	3.78 (1.64)	$t(18) = 1.25$
I attended training sessions because I knew I would be reimbursed for my time	3.00 (1.10)	3.67 (1.00)	$t(18) = 1.41$
I did not attend sessions because I thought they were not useful	1.55 (0.69)	1.33 (0.50)	$t(18) = 0.77$
I attended more sessions because of the attendance bonuses for each training session	2.82 (1.08)	3.78 (1.20)	$t(18) = 1.88$
Acceptability of intervention frequency and intensity			
The training sessions took too much time	1.82 (0.87)	2.44 (0.88)	$t(18) = 1.59$
It was difficult to come in 2 times each week for sessions	1.91 (1.22)	2.11 (0.93)	$t(18) = 0.41$
I could have come in for more sessions	3.64 (1.36)	3.33 (0.71)	$t(18) = 0.60$
Having more sessions would have been helpful	3.73 (1.19)	3.11 (0.60)	$t(18) = 1.41$
There were too many training sessions	2.00 (0.77)	2.44 (0.88)	$t(18) = 1.20$

Note. Standard deviations are presented in parentheses after the mean.

$^*p < 0.05$;

[a]CON $n = 9$ because one participant did not complete post; participants rated each item on a 5-point scale (1 = *Strongly disagree*, 2 = *Disagree,* 3 = *Neutral*, 4 = *Agree*, 5 = *Strongly agree*);

standard deviations are shown in parentheses; ACT = Active Cognitive Training; CON = Control Training.