

A Brief Report of an Executive Functioning Training Pilot RCT in Adults with HIV: A Descriptive Case Comparison Study

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Background and Purpose: Cognitive intra-individual variability (IIV) refers to the fluctuations observed in cognitive performance. The aim of this article was to characterize and describe for illustrative purposes an approach to administer executive functioning training to people living with HIV (PLWH) to reduce their cognitive IIV. This brief report highlights four cases in an on-going study investigating cognitive IIV in HIV. In HIV, cognitive IIV has been associated with cognitive decline, cortical atrophy, and mortality risk. The Executive Dysfunction Hypothesis suggests improving executive functioning could reduce cognitive IIV.

Study Design: In the parent on-going pilot RCT (called the Executive Functioning Training (EFT) Study), 120 PLWH are randomized to either a no-contact control group or an executive functioning training group which receives 20 hours of computerized exercises. To characterize this study, this article describes an interim descriptive case analysis (N = 4) that was conducted with the first two participants who completed training (n = 2) and compared to demographically matched control (n = 2) participants.

Results: Using the Connor's Continuous Performance Test 3rd Edition, results showed improvements in reaction time (*Hit RT*, by -24.5 points) and cognitive IIV (*HRT SD*, *Variability*, by -16 points) in the training group compared to the no-contact control group. In other words, the training appeared to reduce cognitive IIV.

Conclusion: This finding suggests that by improving executive functioning through executive functioning training, this may stabilize cognitive functioning in general, as indicated by reduced cognitive IIV. Although preliminary, these encouraging results support the Executive Dysfunction Hypothesis and suggests further exploration of cognitive IIV may provide insights on how to improve cognition in aging PLWH. Implications for neuroscience nursing are provided.

Plain Language Summary: People living with HIV (PLWH) may experience more cognitive fluctuation which interferes with performing instrumental activities of daily living (IADLs). When our cognitive abilities fluctuate a lot, a phenomenon called cognitive intra-individual variability, this can affect how well we perform everyday activities such as driving a car or paying attention to a TV program. In fact, cognitive fluctuation can impact whether an activity is performed correctly or completed at all. If we can reduce cognitive fluctuation, we might be able to improve everyday functioning. We tested whether PLWH receiving 20 hours of cognitive training, called executive functioning training, can reduce such cognitive fluctuation. We compared two participants who received the cognitive training to two participants who did not. Those who received the cognitive training had less cognitive fluctuation. Although more participants are needed to determine whether this cognitive training is helpful, these findings are encouraging. Perhaps this cognitive training can reduce cognitive fluctuation and improve everyday functioning such as remembering to take one's medications or performing an activity.

Keywords: HIV/AIDS, cognition, cognitive variability, executive function, executive dysfunction

As people living with HIV (PLWH) age, some frequently encounter both medical and behavioral challenges that can impact their ability to age successfully. One significant challenge is decreased cognitive efficiency that can result in HIV-Associated Neurocognitive Disorder (HAND), affecting nearly 44% of PLWH.¹ The seriousness and prevalence of these cognitive impairments (eg, forgetfulness, difficulty with medication adherence) may escalate with the onset of age-related neurological issues (ie, transient ischemic attacks, white matter hyperintensities) and age-related comorbidities known to impact brain function (ie, diabetes, heart disease).^{2–4} These cognitive impairments impact instrumental activities of daily living (IADLs) such as medication adherence and driving safety.⁵ Processes leading to such cognitive impairments remain complex, involving factors like neuroinflammation, depression, substance misuse, and inadequate mental stimulation. Over time, these mechanisms can diminish cognitive reserve and overall brain health, leading to observable cognitive impairments associated with HAND.²

Nurses and allied healthcare professionals seek treatments to protect one from cognitive impairments as PLWH age. Given the complexity of many PLWH being prone to polypharmacy issues and multiple comorbidities (ie, renal and hepatic insufficiency), non-pharmacological treatments are preferred to avoid medical complications. Also, there are no pharmacological approaches shown to produce robust and sustained neurological or cognitive benefits.² Thus, behavioral approaches are preferred.

One behavioral approach in which much evidence has emerged is cognitive training. Cognitive training refers to structured mental exercises specifically designed by neuroscientists that require patients to engage in these exercises, requiring them to use targeted thought processes (often associated with certain brain structures) to complete the exercises; these thought processes approximate certain cognitive skills/domains that can be quantified by specific cognitive performance tests.^{6–8} These cognitive training approaches often target improvement in particular cognitive domains such as speed of processing, working memory, and executive functioning. For example, in a pretest/posttest study of 46 PLWH, participants were assigned to either a no-contact control group or a speed of processing training group. Those in the speed of processing training group underwent 10 hours of specially designed computer games that required swift processing of complex visual information.^{7,9} Compared to the control group, those in the training group experienced improvements in a cognitive measure of speed of processing as well as a measure of everyday functioning. In a systematic review of 13 cognitive training studies in PLWH, researchers found that, in general, cognitive training improved performance in the cognitive domain in which cognitive training occurred (ie, speed of processing training improved speed of processing performance, executive functioning improved executive functioning performance);¹⁰ however, studies were not able to improve global cognition, and these studies were not powered or designed to examine cognitive changes longitudinally. Also, none of these studies incorporated the concept of cognitive intra-individual variability (IIV).

Cognitive IIV refers to the natural fluctuations observed in cognitive performance when the same cognitive test is taken multiple times (referred to as inconsistency) or across different cognitive tests (referred to as dispersion); such variability has been shown to provide predictive value beyond traditional mean-based cognitive measures.^{11–13} In other words, the measure of the spread in variability of cognitive performance may possess more predictive value than the average or summed scores of such cognitive measures. For a hypothetical example, as seen in [Figure 1](#), Jeff and Sam (fictitious names) took a reaction time test and when looking at their average score, they both performed at the same level. We would assume that they are functioning similarly; however, when looking at the spread/variability in their reaction time, we see that Sam had a lot more variability in his reaction time. From what we know about cognitive IIV, this is not a good cognitive indicator for Sam.

Elevated cognitive IIV is suggested to signify poor coordination of cognitive abilities, potentially indicating subtle cognitive decline.¹⁴ This variability in cognitive performance is linked to cognitive impairment and decline across diverse clinical populations. For example, in a prospective cohort comprising 897 community-dwelling older adults (70+ years), Holtzer et al discovered that baseline cognitive IIV (ie, dispersion) was a predictor of developing dementia three years later.¹⁵ This association held true even after adjusting for the mean-based cognitive performance at the initial baseline assessment.

Cognitive IIV also is relevant to the study of neuroHIV. In a systematic review, focusing on 13 neuroHIV studies examining cognitive IIV, researchers concluded that it holds promise as an approach to identify subtle cognitive impairments not captured by traditional mean-based cognition.¹⁴ In PLWH, increased cognitive IIV has been associated

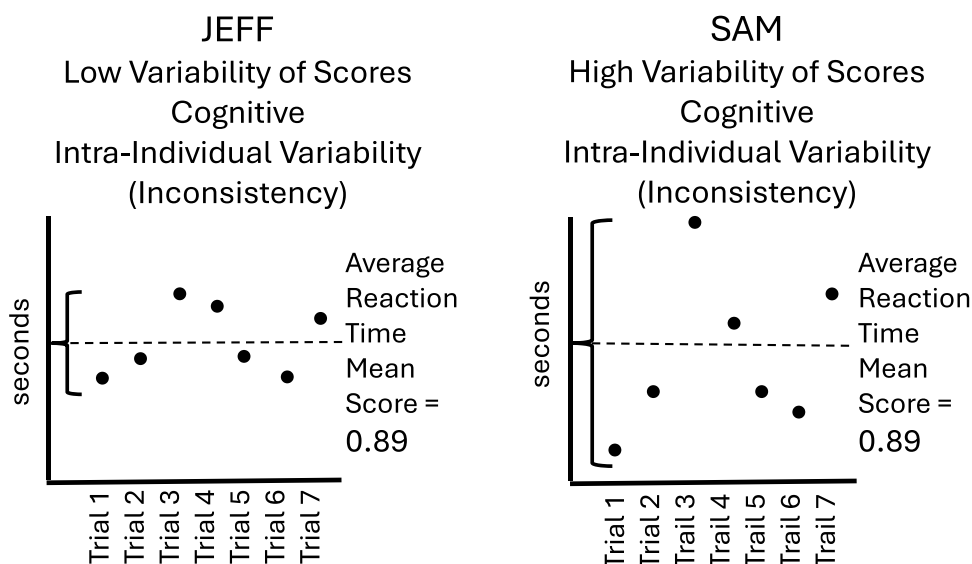


Figure 1 Hypothetical Comparison of Fictitious Cases with the Same Mean Score but Different Cognitive IIV (Variability).

with: 1) poorer cognitive performance and decline over time, 2) cortical atrophy involving both gray and white matter volume, 3) heightened mortality risk, and 4) difficulties in everyday functioning.^{14,16,17}

Given the impact of cognitive IIV in neuroHIV, we proposed using executive functioning training to improve executive functioning which we hypothesized will reduce cognitive IIV. Based on the Executive Dysfunction Hypothesis, it posits that cognitive IIV emerges because there is poor coordination of the other cognitive domains which creates such vicissitudes in cognitive function, and this coordination relies heavily on executive functioning.¹⁴ This point is pertinent; a meta-analysis of 37 studies of PLWH found executive dysfunction may be more pronounced than in those without HIV.¹⁸ Thus, if executive functioning can be improved, perhaps this will reduce cognitive IIV and possibly produce better outcomes. Fortunately, cognitive training studies using executive functioning training have been able to improve this cognitive ability in older adults and those with HIV,^{10,14,19} unfortunately, these studies did not include measures of cognitive IIV.

Based on the above literature, the purpose of this article was to characterize an approach to administer executive functioning training to PLWH to reduce their cognitive IIV. In this study, participants are randomized into either a 20-hour executive functioning training group or a no-contact control group; this is referred to as the Executive Functioning Training (EFT) Study. To contextualize the EFT Study, this current article used a descriptive case comparison approach to describe the treatment outcomes of two participants in the treatment group that received the executive functioning training compared to two participants in the no-contact control group. From this, implications of this study to nursing care for cognitively vulnerable PLWH are provided.

Methods

Study Design

We are examining in an on-going randomized control trial the feasibility of a 2-group pretest/posttest experimental study targeting recruitment of 120 PLWH aged 40+ years (for additional details, see Odii et al).²⁰ This current descriptive case comparison study is a smaller piece of the larger parent EFT randomized clinical trial (on-going). As a descriptive case comparison study, only descriptive analyses are provided of selected cases in the experimental condition and compared to demographically matched cases (ie, case comparison); this is done to illustrate and highlight the basic structure and design of the larger parent study. The first two participants to complete the executive functioning training arm ($n = 2$) were compared to demographically matched participants in the no-contact control group ($n = 2$); their data were analyzed by examining pretest/posttest changes (~12 weeks) in their cognitive IIV

scores and other outcome variables (ie, depressive symptomatology). These cases in the experimental condition were selected because they were the first two who finished all the training protocol including receiving the full dose (ie, 20 hours) of the executive functioning training (ie, consecutively completed the study from the start of the study). Also, they were very representative of the overall sample so far (middle-aged African Americans). Thus, we chose participants in the control group who were most closely aligned to their basic demographics, to methodologically control for these demographic variables. Overall, this is a nested, exploratory, and preliminary comparison of cases selected from the parent trial, conducted for illustrative and hypothesis generating purposes rather than inferential statistical analysis. As this was a descriptive study of a treatment protocol, causal inferences are limited. The EFT Study was approved by the University of Alabama at Birmingham (UAB) Institutional Review Board (IRB-300008561). All participants provided informed consent, in accordance with the Declaration of Helsinki.

Recruitment

In the EFT study, participants were recruited from two sources: 1) recruited via flyers posted at the UAB HIV clinic and 2) the CINCS (Centers for AIDS Research Network of Integrated Clinical Systems) participation list at the same UAB HIV clinic as these participants indicated that they wanted to be recruited and contacted for future studies. With the first source, the flyer had our office number instructing participants to call us to ask for more details. With the second source, study staff called potential participants from the CINCS list. All participants from both recruitment sources were administered a telephone screen to determine whether they met study criteria. Specifically, eligibility criteria were: a) be 40+ years of age; b) be diagnosed with HIV for at least 1 year; c) have no severe neuro-medical comorbidity (eg, schizophrenia); d) be able to drive; e) reside within 60 miles of the research center; f) not be legally blind or deaf; g) able to understand/speak English; h) be stably housed; i) not undergoing radiation or chemotherapy; j) have no history of significant brain trauma; and k) not be diagnosed with COVID-19 within the past 3 months. The rationale for these eligibility criteria were to ensure participants were able to attend in person visits at the research center and to ensure that any cognitive problems present were likely due to HIV and not to other causes (ie, brain trauma). The focus on PLWH in this older age group (40+ years) was prompted by the higher prevalence of cognitive impairments.^{1,2}

Instruments

Administration time of the pretest/baseline and posttest assessments took approximately 2 hours each. Assessments were administered in-person by a trained technician (S.B.) at our university research center. Although not reported in this descriptive case comparison article, there were several measures administered at each assessment that measured quality of life, training satisfaction, cognitive function, and more (for more information, see EFT study protocol article).²⁰ Yet, for this descriptive case comparison study, to contextualize the study we only reported the measures below as they describe the sample demographics, health status, basic educational quality, depressive symptomatology, and reaction time and cognitive IIV measures pertinent to the overall study hypothesis (ie, executive functioning training will reduce cognitive IIV).

Demographics and Health

Basic demographic information (ie, age, gender, ethnicity, education) along with HIV-related clinical data (CD4+T lymphocyte count, HIV viral load) were gathered by self-report at pretest/baseline. We acknowledge self-reported health information is susceptible to poor health literacy/health numeracy and recall bias.²¹

Center for Epidemiologic Studies Depression Scale-Revised (CES-D)

The CES-D consists of 20 items reflective of statements about mood in which participants rate how often they felt that way in the past week ranging from 0 (*rarely or none of the time*) to 3 (*most or all of the time*). These were tallied with total scores ranging from 0–60; a score of ≥ 16 indicates clinically relevant depressive symptomatology.²²

Connor's Continuous Performance Test (CCPT; 3rd Edition)

The CCPT is a widely accepted test of sustained/selective attention and impulsivity; it is commonly used in the cognitive IIV literature and produces IIV inconsistency coefficients as well as several measures of reaction time, attention, inhibition, and impulsivity.²³ The CCPT instructs participants to swiftly press the space bar whenever a non-“X” letter (ie, target) appears on the screen, aiming for the fastest response. Additionally, participants are

required to withhold this response when the letter “X” (ie, non-target) is presented. Targets (non-“X” letters) make up 90% of the letters presented. Each letter is displayed for 250 ms, and there is an inter-stimulus interval (ISI) of 1, 2, or 4 seconds between letters. The complete test consists of a 1-minute practice block and approximately 14 minutes of testing, divided into six blocks. Each block can be further divided into three sub-blocks of 20 trials, each with a specific ISI set to 1, 2, or 4 seconds. CCPT outcome variables are represented as *t*-scores, standardized by age and gender. Lower *t*-score values indicate better performance, reflecting quicker or more consistent responses. There are 13 values produced from the CCPT, but not all are relevant for this descriptive analysis; thus, seven are reported and for all of them, higher scores indicate worse performance. 1. *Detectivity (d')* – This measure indicates how well participants discriminate targets from non-targets. 2. *Omissions (%)* – Considered an indicator of inattentiveness, it measures how many targets were missed. 3. *Commissions (%)* – Considered an indicator of impulsivity, it measures the number of incorrect responses to non-targets. 4. *Perseveration (%)* – Considered an indicator of impulsive, anticipatory, or repetitive responding, it measures how many responses occur within 100 ms following the presentation of a stimulus. 5. *Hit Reaction Time (HRT)* – This measure is the only indicator of response time (RT) central tendency. 6. *HRT Standard Deviation (HRT SD)* – A measure of inconsistency, this measure denotes the standard deviation of the participant’s *Hit RT* across all test trials. 7. *Variability* – This measure represents the standard deviation of *Hit SD* across trial sub-blocks; this is considered one of the other main inconsistency indices.

Intervention

We maintained a stratified randomization method with permuted block and treatment allocation between African Americans/Caucasians, men/women, and low/high cognitive IIV scores (cutoff = 55 on the HRT SD (Hit Rate Standard Deviation) on the Connor’s Continuous Performance Test (Version 3 (CCPT-3)). This intervention was described in the consent form and then once assigned to the intervention, participants were described the cognitive training more. During the training sessions, participants were personally shown how to engage in the cognitive training by the trained technician (S.B.) who answered questions; this staff person also checked in on the participant frequently during the training sessions to answer any questions that arose. Otherwise, the training software was designed to be self-administered and it provided instructions and prompts to facilitate the training exercises.

Those assigned to the EFT group were assigned to 20 hours of complex mental exercises requiring one to set shift, that is to maintain at least two sets of rules and decide which is appropriate to determine the correct response. For example, in “Mind Bender” the participant is presented two rules. The first rule might be when presented the spelling of two different numbers, select the word that spells the highest number (“seven” vs “four”). But the second rule might be when presented two digits, select the lowest number (“4” vs “7”). Participants will be presented pairs of either words or digits of number where they have to make this selection as quickly as possible, based on either the first or second rule. The effect size for EFT from a prior HIV cognitive training study using these exercises was large ($d = -0.89$).⁸ The exercises were created by BrainHQ (POSIT Science Inc). The training consisted of four modules. One, “Mind Binder” is a “set shifting” exercise where one is presented with two rules, but one must choose the correct answer based upon the rules provided in this exercise (explained above). Second, “Mixed Signals” requires one to listen to a number, letter, or other information while looking at a similar set of information. For example, in one version of this, one might hear the word “four” but is visually presented “444”, since there are not four digits, one does not respond and waits for the next presentation; but in the next presentation one might hear the word “three” but is presented “444” and since there are three digits, one presses the “YES” button as soon as possible. Variations and rules of this change while one must ignore competing information; this exercise is similar to the Stroop test. Third, “Card Shark” is an extension of a visual n-back paradigm using an aspect of executive functioning (ie, working memory). More specifically, participants are presented standard playing cards which are added sequentially, one at a time. The card is presented one at a time, and the participant must decide if the current card that is flipped over matched the one just presented. After this mastery, this exercise becomes more difficult and one must decide if the current card that is flipped over matched the one presented two back (or more for later levels) in the sequence. And fourth, “Freeze Frame” is an extension of the go/no go paradigm using an aspect of executive functioning (ie, working memory). Participants are shown a target image and then a series of other images that may or may not match the target. If the presented image does not match the target, they are instructed to click “NO” but if it does match the target, they are instructed to “freeze”, that is, do nothing and wait for the next image to be



Figure 2 Executive Functioning Training Exercises.

presented. For these four exercises, participants could train up to two hours at a time at our research center. Participants spread out their training over several weeks to fit their schedule. A picture of the software and gaming features is available in [Figure 2](#).

Data Analysis

We chose the first participants who completed the executive functioning training and then selected two other participants in the no-contact control group who were the closest demographic match to the first two participants. A descriptive pretest/posttest comparison of these cases was constructed ([Table 1](#)) to examine changes in CCPT scores, with particular

Table 1 Case Comparisons Between the Executive Functioning Training Group and the No-Contact Control Group

Variable	Case A	Case B	Case C	Case D	Between Group Observations
	Executive Functioning Training Group		No-Contact Control Group		
Age	45	57	45	58	Participants are demographically similar.
Sex	Female	Male	Female	Male	
Race	AA	AA	AA	AA	
Education (years)	11	14	16	16	
Income (years)	0–10K	0–10K	80–90K	20–30K	
HIV Viral Load (self-reported)	<50	<50	<50	<50	Those in the training group had higher depression.
CES-Depression*					
Baseline	16	27	9	14	
Posttest	21	30	14	8	
Change	+8	+3	+5	–6	
CCPT Detectability (d')					The training group improved slightly more than controls (–5.5 pt. difference).
Baseline	43	56	61	63	
Posttest	29	41	48	58	
Change	–14	–15	–13	–5	
CCPT Omissions					
Baseline	45	59	64	58	The training group did not improve more than controls (2 pt. difference).
Posttest	44	45	47	56	
Change	–1	–14	–17	–2	

(Continued)

Table 1 (Continued).

Variable	Case A	Case B	Case C	Case D	Between Group Observations
	Executive Functioning Training Group		No-Contact Control Group		
CCPT Commissions					The training group did not improve more than controls (3 pt. difference).
Baseline	42	46	53	56	
Posttest	36	44	46	49	
Change	-6	-2	-7	-7	The training group did not improve more than controls (-3.5 pt. difference).
CCPT Perseveration					
Baseline	46	45	46	83	
Posttest	46	45	46	90	The training group improved more than controls (-24.5 pt. difference).
Change	0	0	0	+7	
CCPT Hit RT					
Baseline	78	61	49	68	
Posttest	56	47	55	75	
Change	-22	-14	+6	+7	
CCPT Hit SD [†]					The training group improved more than controls (-16 pt. difference).
Baseline	82	57	56	60	
Posttest	48	49	49	57	
Change	-34	-8	-7	-3	The training group improved more than controls (-9 pt. difference).
CCPT Variability [†]					
Baseline	53	68	69	74	
Posttest	42	48	59	71	
Change	-11	-20	-10	-3	

Notes: + = cognitive change favoring the control group; - = cognitive change favoring the training group; [†] = these are considered the primary cognitive IIV (ie, inconsistency) measures.

Abbreviations: AA, African American; Education (year) = 12 (high school graduate or equivalency), 13 = Associate's degree, 16 = Bachelor's degree; CCPT, Connor's Continuous Performance Test 3rd edition; CES-D, Centers for Epidemiological Studies – Depression scale (*A score of 16 or higher is indicative of clinically significant depressive symptomatology); DK, do not know; RT, reaction time; SD, standard deviation; WRAT, Wide Range Achievement Test (a measure of educational quality).

focus on the cognitive IIV scores of *HRT SD* and *Variability*. Our statistician developed and generated the comparisons by: 1) calculating the change within each participant, 2) then averaging those changes for each group, and 3) then calculating the point difference in change (EFT – Control). Positive point difference scores reflect therapeutic benefit attributed to the control condition, and negative point difference scores reflect therapeutic benefit attributed to the training condition. Absolute value higher point different scores indicate more therapeutic benefit.

Results

As seen in Table 1, all four cases were African Americans 45 to 58 years of age. Participants by and large did not know their CD4+ T lymphocyte count > 200 cells/mm,³ but all reported being undetectable. Both participants in the executive functioning training group received the full training (ie, 20 hours of training). Compared to the no-contact control group, those in the executive functioning training group had higher levels of depressive symptomatology at baseline and posttest; the training did not appear to reduce these symptoms. Using the absolute value point difference scores of 5 or greater for the CCPT as a cut-off, compared to the no-contact control group, it appears that those in the executive functioning training group experienced benefits on *Detectability (d')* (by -5.5 pt difference) and *Hit RT* (by -24.5 pt difference). Furthermore, for the two indicators of cognitive IIV, *Hit SD* and *Variability* showed marked improvements compared to the no-contact control group by a -16 point difference and a -9 point difference, respectively. Negligible changes were observed for *Omission*, *Commissions*, and *Perseveration*. These results were novel because this is the first time (to our knowledge) that any study has been designed to specifically address and reduce cognitive IIV in any

population. The fact that this descriptive case comparison study found reductions in Hit RT and other variability metrics was encouraging.

Discussion

Our interim descriptive case comparison study suggests an emerging pattern of improvement on cognitive variables of discrimination (*Detectivity*) and reaction time (*Hit RT*) as well as cognitive IIV (*HRT SD*, *Variability*) resulting from the executive functioning training. Based on the Executive Dysfunction Hypothesis, cognitive IIV may result from executive dysfunction; more specifically, as executive function is considered a foundational cognitive ability that directs and orchestrates the use of other cognitive functions, if executive functioning is compromised, this will exert downstream effects whereby one has poor coordination of other cognitive abilities resulting in cognitive IIV; this in turn would compromise everyday functioning. Thus, by improving executive functioning through computerized executive functioning training, this could strengthen such cognitive abilities that may harmonize cognitive functioning across and within cognitive domains.

Although these preliminary findings are promising, clearly more research is required such as how much training (ie, dosage) is needed to achieve this goal of reducing cognitive IIV, whether it be 10 hours, 20 hours, or 50 hours. In a meta-analysis of 52 cognitive training studies in older adults (combined $N = 4,885$), Lampit et al suggested that 20 hours seems to be the optimal training amount in general as more than that introduces training fatigue.²⁴ That is an important consideration as such training can be very intense and requires much focus on the part of the participant. But that may not apply to all types of cognitive training; for example, improving executive functioning could require more time to accomplish than trying to improve another cognitive domain such as psychomotor ability. In fact, that might explain why the literature reports different training effect sizes of different cognitive domains because some may require more training time (dosage) to change than others. Although the parent EFT study will not be able to resolve these issues that are pernicious in the cognitive training literature, it will add to the literature by providing information about the efficacy of using 20 hours of executive functioning training in a population of PLWH.

Another consideration is how robust will the training effect be over time (eg, weeks, months, or years) as such training effects may fade without being boosted with additional training sessions. In a large study of community-dwelling older adults (without HIV), Edwards et al found that 10 hours of speed of processing training was quite robust overtime, resulting in a remarkable reduction in the prevalence of dementia (by 29%) over a span of 10 years when compared to a control group.²⁵ This highlights the impressive long-term advantages of cognitive training. Unfortunately, our EFT Study was not designed to ascertain the sustained duration of cognitive benefits from such training.

Strengths and limitations of this descriptive case comparison study are as follows. First, given the pilot nature of our study, a small sample was used to describe the protocol so inferences cannot be concluded; albeit, the preliminary findings are meant to provide insights and generate discussion. Second, participants in the experimental group had higher levels of depressive symptomatology at baseline and posttest compared to the cases in the control group. It is not clear why those two participants randomized to the experimental condition would have such higher levels of depressive symptomatology; we assume this is just random. Participants were randomized after the baseline assessment, so being randomized to the experimental condition would not have exerted an influence on depressive mood. Interestingly, although depressive symptomatology has been shown to negatively affect cognition,²⁶ those in the experimental condition still improved on some of the measures of cognition and cognitive IIV. Third, clinical and statistical significance cannot be determined at this time given the pilot nature of this study. As there are only 4 cases, we cannot make inferential (ie, statistically significant) conclusions as such inferential statistics would require larger samples sizes. Nor can we, at this time, provide definitive statements of whether the improvements are clinically significant as we do not have enough sample size to calculate whether the reductions in cognitive IIV are correlated to medication adherence or other clinically relevant measures. But once the study is over and the data analyses are available in the next year or two, we will be able to answer this question more definitively. Fourth, the follow-up assessment was only ~12 weeks at immediate posttest; the effects may fade over time but the study was not designed nor funded to look at a longer follow-up assessment. A longer follow-up assessment would be important to detect if the training effects are robust over time.

Finally, this is a unique descriptive case comparison study that highlights and portrays an innovative cognitive training approach using cognitive IIV as an impetus for training; this is a unique contribution to the neurocognitive field.

As the parent EFT Study continues, a larger sample from this feasibility RCT will be available to determine whether executive functioning training is effective in improving executive functioning and likewise reducing cognitive IIV, measured by inconsistency and by dispersion. To our knowledge, this is the first study to attempt to reduce cognitive IIV and measure such change with both measures of cognitive IIV. Furthermore, given the relationship between cognition and everyday functioning and quality of life, the EFT study will explore whether changes in cognitive IIV translate into these non-cognitive therapeutic benefits for PLWH.

Nursing implications for practice and research are noted. First, if the EFT approach can truly change cognitive IIV, this may improve overall cognition as well. As nurses and allied health professionals seek ways to improve successful cognitive aging in PLWH,² this is an approach they can educate their patients. Second, if the EFT approach can also improve everyday functioning such as medication adherence or driving an automobile, this could have real world applications in which nurses can provide clinical recommendations for use. In fact, studies do show that cognitive IIV is related to IADLs.²⁷ And third, for nurse researchers who study neurological complications from HIV and other conditions, the use of this EFT approach may produce positive clinical outcomes (ie, improved medication adherence).

Conclusion

In conclusion, nurses and allied health professionals need therapeutic strategies for their patients to reduce the risk of cognitive impairment as PLWH age. Fortunately, prior research has already shown that EFT can improve this cognitive ability, but it is unknown whether it can change cognitive IIV also. Given that cognitive IIV is lauded as a more salient predictor of cognitive decline and poorer outcomes in PLWH than mean-based cognitive measures, it is hoped that by reducing cognitive IIV as well as the underlying neurological sequelae surrounding it, we will be able to alter the trajectory of such detrimental cognitive outcomes. This approach is, as it should be, being tested in a much larger RCT study; the parent EFT study will allow us to determine whether this cognitive training improves executive functioning, reduces cognitive IIV, and improves everyday functioning such as medication adherence and self-reported IADLs. It will also be important to conduct long-term follow-up assessments to determine how robust the treatment effect is over time; if it is not, perhaps booster cognitive trainings would be needed. This EFT approach may be tested in other clinical populations in which cognitive IIV is shown to be elevated, such as breast cancer survivors.²⁸ At the intersection between nursing care and neuroscience, this cognitive IIV approach represents an innovative step in addressing these complex neurological issues in HIV care. In fact, despite the pilot nature of our study, this approach may be suitable and adaptable to other clinical populations.

Data Sharing Statement

These data pertaining to this case comparison study are available upon request to the corresponding author. These data will be deidentified. Data collection forms are also electronically available upon request. These data will be available for the next 5 years after the publication data of this article.

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Author Contributions

All authors meet the following IMCJE criteria: 1) Made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; 2) Have drafted or written, or substantially revised or critically reviewed the article; 3) Have agreed on the journal to which the article will be submitted; 4) Reviewed and agreed on all versions of the article before submission, during revision, the final version accepted for publication, and any significant changes introduced at the proofing stage; and 5) Agree to take responsibility and be accountable for the contents of the article.

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Disclosure

The authors report no conflicts of interest in this work.

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