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The Effects of Speed of Processing Training and Transcranial Direct Current Stimulation on Global Sleep Quality and Speed of Processing in Older Adults with and without HIV: A Pilot Study

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Abstract

Some older adults with HIV experience poor sleep which can worsen cognition. Transcranial direct current stimulation (tDCS) and cognitive training have improved sleep and cognition in studies of older adults; yet their combined influence is unknown in adults with HIV. Older adults with HIV ($n = 33$) and without HIV ($n = 33$) were randomized to receive 10 one-hour sessions of speed of processing (SOP) training with tDCS or sham tDCS over approximately 5 weeks. tDCS with SOP training did not improve sleep. Omitting correction of multiple comparisons for this exploratory pilot study, main effects for HIV ($F[1, 59] = 5.26$, $p = .03$, $\eta_p^2 = .082$) and tDCS ($F[1, 59] = 5.16$, $p = .03$, $\eta_p^2 = .080$) on the Digit Copy Test were detected. A HIV x tDCS interaction was detected on the Letter Comparison Test ($F[1, 59] = 5.50$, $p = .02$, $\eta_p^2 = .085$). Useful Field of View scores improved across all four groups ($F[1, 59] = 64.76$, $p < .001$, $\eta_p^2 = .523$). No significant effects for HIV ($F[1, 59] = 1.82$, $p = .18$) and tDCS ($F[1, 59] = .01$, $p = .94$) were detected on the Useful Field of View test. While the current study did not show effects of combined tDCS and SOP training on sleep quality, future studies are needed to examine the effects of such interventions on sleep-related cognitive functions among those cognitively impaired adults with HIV.

Keywords

HIV; Aging; Sleep Quality; Cognitive Interventions; Cognitive Functioning

As the life expectancy of adults with HIV approaches normal (Lewden et al., 2012), challenges with cognitive functioning persist. By some estimates, 52%−59% of adults with

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HIV experience HIV-associated neurocognitive disorders despite the use of combination antiretroviral therapy (cART) (Bonnet et al., 2013; Heaton et al., 2010). Given adults age 50 and older will comprise 70% of the HIV population by 2020 (U.S. Special Senate Committee on Aging, 2013), concerns mount that the effects of HIV-related neuroinflammation and the process of aging may negatively impact cognitive functioning. While there are multiple contributors to poor cognitive functioning, some age-related changes in sleep quality may influence cognition. Interventions targeting sleep quality should be examined in efforts to facilitate better cognitive functioning.

Compared to the general population, some studies suggest there is a higher prevalence of sleeping problems among adults with HIV (Taibi, 2013; Wibbeler, Reichelt, Husstedt, & Evers, 2012). In a study of adults with HIV (n = 180) and without HIV (n = 120), Wibbeler and colleagues (2012) found that compared to adults without HIV, daytime sleepiness was higher (46.6% versus 19.4%), and the percentage of those with poor sleep quality was higher (63.9% versus 21.0%) in adults with HIV. Although there are numerous factors that contribute to differences in sleep quality, some adults with HIV may be more sensitive to physiological (e.g., immunological state and effects of antiretroviral medications) (Allavena et al., 2014) and socio-psychological changes such as stress of an HIV diagnosis and lack of employment (Vance et al., 2015) that may adversely affect their sleep quality. Unfortunately, poor sleep quality can worsen cognitive function in multiple domains. Also, poor cognitive function and increased neuroinflammation over time can aggravate sleep quality.

Sleep and Cognitive Functioning

According to the synaptic homeostasis hypothesis, sleep plays a functional role in synaptic plasticity or strengthening of neuronal connections and promotes growth of new neurons in the hippocampus, particularly the dentate gyrus which involves the formation of memories (Stickgold & Walker, 2013; Tononi & Cirelli, 2014). Poor sleep quality inhibits restoration of cortical regions of the brain, primarily the prefrontal cortex, which is necessary for the brain to perform higher level cognitive processes such as executive functioning (Plessis et al., 2014). Given adults with HIV are susceptible to cortical (e.g., cerebral cortex) and subcortical atrophy (e.g., basal ganglia) (Kuper et al., 2011), the effects of poor sleep quality on such areas may be more severe and negatively impact cognitive function. In some adults with HIV, atrophy of subcortical regions of the brain such as the basal ganglia may alter neurotransmitter levels involved in sleep regulation (e.g., serotonin) which can compromise sleep quality (Yaffe, Falvey, & Hoang, 2014). Therefore, those with HIV who have preexisting problems (e.g., mood disorders) regulating neurotransmitter levels may be more susceptible to poor sleep quality which may further impair cognitive functioning (Cody & Vance, 2016).

Cognitive Training and Sleep Quality

Cognitive training, which involves focused learning, may increase the demands for sleep, and thus induce it (Haimov & Shatil, 2013). Sleep may help restore the brain in preparation for later use of higher level cognitive processes (Tononi & Cirelli, 2014). The effects of cognitive training on sleep quality have not been examined in adults with HIV; however,

Haimov and Shatil (2013) examined such effects after randomizing older adults with insomnia to a cognitive training group (n = 34) or a control group (n = 17). The cognitive training group completed a home-based computerized cognitive training program (CogniFit®), which consisted of 21 different training tasks that varied in level of difficulty. The control group completed basic computer tasks (e.g., reading, copying texts, changing font, drawing, and coloring pictures) in Microsoft Word and Paint. Both groups performed three 20–30 minute sessions per week with a no-training day in between sessions for a period of 8 weeks. At baseline and posttest, participants were asked to wear an actigraph for one week to monitor sleep patterns and examine changes in total sleep time, sleep onset latency, sleep efficiency, wake time after sleep onset, and total number of awakenings. Also, the participants were asked to keep sleep diaries during actigraphy monitoring for precise measurement of sleep quality. Compared to the control group who performed basic tasks in Microsoft Word and Paint, the cognitive training group showed improvements in sleep quality (i.e., sleep onset latency and sleep efficiency). In addition, better concentration was associated with an increase in the duration of sleep which suggests that sleep may influence attention span (Haimov & Shatil, 2013). Also, Haimov and Shatil's findings suggest that sleep may depend on keeping the brain active. Therefore, cognitive training may lead to cognitive exertion which can increase one's demand for sleep.

Similarly, speed of processing (SOP) training is a computerized cognitive intervention designed to increase the speed and accuracy in which participants visually perceive certain stimuli (Ball, Edwards, & Ross, 2007). A series of tasks involve identifying a target object in the center of the monitor and simultaneously locating another object in the periphery. The tasks become increasingly difficult and are adjusted based on the individual's performance level (an easier task is presented when a task is performed incorrectly, and a more difficult task is presented when a task is performed correctly). In concurrent tasks of visual discrimination and attention, objects are presented at faster speeds and embedded among distractors. The Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) Study was one of the largest studies of cognitive training and everyday functioning outcomes in older adults. Findings from this study showed, compared to memory and reasoning training, SOP training improved cognition and instrumental activities of daily living and these gains were sustained for 10 years post-training (Ball et al., 2007; Rebok et al., 2014). For these reasons, in the current study SOP training was chosen as the most robust cognitive training that may yield the strongest neural benefit to facilitate better sleep.

Transcranial Direct Current Stimulation and Sleep Quality

To date, the effects of transcranial direct current stimulation (tDCS) on sleep quality in adults with HIV have not been examined. However, studies have shown positive effects of tDCS on sleep quality in adults with other comorbidities such as bipolar disorder (Minichino et al., 2014). tDCS is a non-invasive technique that uses static direct electrical currents to stimulate the brain, thereby subtly altering membrane potential of neurons (Brunoni et al., 2012). tDCS involves the application of a low (≤ 2 mA) direct current to the scalp using two electrodes, the anode and cathode. The anodal electrode or positive charge is positioned where the current will enter the brain and excite underlying neurons; whereas, the cathode or negative charge is positioned where the current will exit and reduce excitability of neurons

(Brunoni et al.). Several studies support the use of anodal tDCS for cortical excitability and targeting the dorsal lateral prefrontal cortex (DLPFC), which according to the 10/20 International Positioning System is located around F8 or F10 (right temple above the sphenoid bone). Also, some studies have shown that stimulation of specific areas of the brain using anodal tDCS can improve sleep quality. For example, Minichino and colleagues (2014) found that placement of the anode (stimulatory electrode) on the left prefrontal area with the cathode (inhibitory electrode) on the right cerebellar cortex improved subjective sleep quality in euthymic bipolar patients. Perhaps, concurrent stimulation of certain brain areas using anodal tDCS and a demanding cognitive training protocol such as SOP training may lead to cognitive exertion, and thereby increase the demands for sleep. In addition, this novel approach may enhance noncognitive gains (e.g., protection from depression, better self-rated health) observed from SOP training alone (Vance, Humphrey, Nicholson, & Jablonski-Jaudon, 2014). Hence, such benefits may also improve sleep health in older adults with and without HIV.

Purpose

The current study was designed to examine global sleep quality and SOP in older (50+) adults with and without HIV who received tDCS or sham tDCS with SOP training. The study was conducted to address the following two research aims: Aim 1 – Examine changes in global sleep quality and SOP among older adults with and without HIV who received tDCS or sham tDCS with SOP training (controlling for age, education, and baseline scores); Aim 2 – Examine correlations between change scores for global PSQI and SOP measures by training group.

For Aim 1, it was hypothesized that older adults that received tDCS with SOP training, regardless of HIV status, will have more improvements in sleep quality and SOP. Given that poor sleep and cognitive impairments are common among older adults with and without HIV, both groups may benefit from the potential effects of the combined intervention. However, since adults with HIV have certain cognitive vulnerabilities, this study compares the effects of tDCS and SOP training in adults with and without HIV. For Aim 2, it was hypothesized that changes in sleep quality would positively correlate with changes in SOP by training group. Therefore, improvements in sleep quality would correlate with improvements in speed of processing, and declines in sleep quality would correlate with declines in speed of processing. This hypothesis was based on the bi-directional relationship between sleep and cognitive function.

Methods

Design Overview

In this study of adults with and without HIV, stratified randomization (a balanced protocol using race, gender, and baseline SOP performance) was used to assign participants to one of four groups: 1) HIV-positive tDCS, 2) HIV-positive sham tDCS, 3) HIV-negative tDCS, and 4) HIV-negative sham tDCS. All groups concurrently received SOP training (10 one-hour sessions) with either sham or active tDCS over a period of approximately 5 weeks.

Participants received a baseline and immediate posttest comprehensive neurocognitive battery.

Participants

Permission was obtained from the University of Alabama at Birmingham (UAB) Institutional Review Board to enroll participation from older adults in the community and the UAB 1917 HIV/AIDS Clinic. This pre-post experimental study targeted two groups: adults age 50 and older with and without HIV. Participants were recruited by word of mouth, flyers, and an online ad. Potential participants were instructed to call the study coordinator who then screened them to determine if they met study criteria. Participants were excluded for the following: younger than 50 years of age; homeless; unable to speak and understand English; mentally impaired (e.g., Alzheimer's disease, dementia, or mental retardation); deaf or blind; having experienced brain trauma with loss of consciousness greater than thirty minutes; having other significant neuromedical diagnosis (e.g., schizophrenia, epilepsy, or bipolar disorder); currently receiving chemotherapy, radiation, or dialysis; undergoing treatment for depression, anxiety, or other mood disorders; being left-handed; having intracranial metal plate implants; having a pacemaker or other biomedical device; having previously participated in SOP training; having untreated hypertension; not being a licensed driver; and/or lacking experience using a computer mouse. The only differences between criteria for HIV+ and HIV-samples was the HIV+ criteria did not exclude those without a driver's license or without experience using a computer mouse; however, they were excluded if they have not been diagnosed with HIV for at least 1 year to minimize other confounders that may affect cognition such as reactive depression (Vance, Struzick, & Burrage, 2009). Eligible participants were scheduled an appointment for a baseline visit, after which they were randomized to either sham tDCS or active tDCS groups.

Intervention

A newer version of the SOP program, BrainHQ, was used in this study. Participants were asked to play two games at our lab, Double Decision and Target Tracker, for 1 hour twice a week over a period of 5 weeks (10 training sessions total). In Double Decision, participants were presented an object (car/truck) in the center of the computer monitor and a Route 66 sign in one of several peripheral fields at various speeds, and then asked to identify which central object (car/truck) was presented and the location of the Route 66 sign (see Figure 1). When participants performed the exercise correctly, the speed at which the objects were presented increased and then the objects were embedded among distractors, thus making the task more difficult. When participants performed the exercise incorrectly, the correct answer was displayed on the computer screen and the exercise automatically decreased in speed. This double-staircase technique allowed participants to perform the SOP exercises at their maximum threshold level. Based on their initial performance, if participants improved in subsequent exercises, they could proceed to levels that were more challenging. If participants did not improve, they were given the option to replay the game to increase their score at the current level.

Also, the participants played a game called Target Tracker (see Figure 2). In this game, participants were initially presented one or more objects (balls or jellyfish) and asked to

watch the objects as they moved across the screen among several other balls or jellyfish. When the objects stopped moving, participants were asked to identify the original objects locations. If participants correctly identified the original objects location, they were presented an additional object the next trial. If participants incorrectly identified the original objects, they were presented fewer objects the next trial. At the end of each set of exercises, those who improved their score had the opportunity to move up to the next level which required participants to identify a greater number of objects. However, participants who did not improve could replay the previous level to try and increase their score. Anytime during the hour, participants could alternate between playing Double Decision and Target Tracker; hence, these exercises were designed to improve visual SOP and divided attention.

tDCS

Previously, Clark and colleagues (2012) found that stimulation of F10, the right frontal cortex, increased learning and correlated with improvements in correctly identifying concealed objects. Similarly, this single-blind pre-post study adopted the tDCS protocol used by Clark and colleagues (2012) to examine the effects of tDCS with SOP training on SOP and sleep quality. In this study, a 4 cm^2 sponge electrode was placed over the right inferior frontal cortex near F10 and the cathode electrode was placed on the contralateral upper arm. The participants in the active tDCS group received a 2.0 mA current for 20 minutes while engaging in SOP training. After such time, the current was turned off although the participants continued to engage in the SOP training until the end of the hour. Similarly, those in the sham tDCS condition had an identical protocol except they received the 2.0 mA current for only 30 seconds, and then the strength of the current ramped down to 0 mA. During the training, participants were asked to describe the physical sensation of the tDCS after 5 minutes and 15 minutes using the following descriptors: “0) no sensation, 1) cold, 2) some tingling, 3) warm, 4) lots of tingling/some itching, 5) very warm, 6) lots of itching, 7) burning (like a sunburn), 8) burning (like scalding water), 9) ‘hurts a lot’” (Clark et al. 2012, p.120). If participants indicated a 7 or higher, they were given the option to continue or reduce the stimulation. One participant in this study indicated a sensation of 7 or higher and her tDCS amperage was reduced to a level she could tolerate. Otherwise, participants completed 10 hours of training at the center using the aforementioned combined SOP and tDCS training protocols.

Study Measures (Baseline and Posttest)

Prior to beginning the study, informed consent was obtained from participants. The baseline and posttest assessments were 2.5-hour visits. At baseline, several measures were used to gather background information and assess sleep quality and cognitive ability. Sleep quality and cognitive ability were reassessed at posttest.

Demographic Questionnaire.—This experimenter-generated measure was used to gather information on age, gender, race (0 = minority, 1 = nonminority), household income before taxes (1 = $0 – $10K; 2 = $10,001 – $20K; etc), and years of education.

Pittsburgh Sleep Quality Index.—The PSQI, a questionnaire consisting of 19 items, was used to measure participants’ sleep quality in the past month. The seven subscales of

PSQI include sleep efficiency, sleep duration, sleep disturbance, sleep latency onset, sleep medication use, and daytime dysfunction due to sleepiness. Using a Likert-type scale (0 = *not at all,* 1 = *less than once a week,* 2 = *two or more times a week,* and 3 = *three or more times a week*), participants were asked to what extent do various factors such as waking up in the middle of the night interfere with their sleep. Scores from the subscales were summed to yield a global score ranging from 0 to 21, with scores greater than 5 indicating poor sleep quality. In a study of 80 patients with primary insomnia, test-retest reliability was 0.87 (Backhaus, Junghanns, Broocks, Riemann, & Hohagen, 2002).

Letter and Pattern Comparison Test.—These two paper-and-pencil tests measured SOP. In the Letter Comparison Test, participants were presented two sets of letters containing three (e.g., HLV, HLX), six (e.g., NLCVZL, NLCVZL), or nine (e.g., SLNFZHMBQ, SLHFZNMBQ) segments. Given 20 seconds per section (6 sections), participants were asked to write as quickly as possible a “S” if the segments were the same or “D” if the segments were different. The score was the total number of correct responses ranging from 0 to 192, with higher scores indicating faster SOP (Salthouse, 1991). Similarly, the Pattern Comparison Test consisted of 96 pairs of patterns containing three, six, or nine line segments. Given 20 seconds per section (3 sections), participants were asked to write as quickly as possible a “S” if the patterns were the same or “D” if the patterns were different. The score was the total number of correct responses ranging from 0 to 96, with higher scores indicating faster SOP (Salthouse, 1991).

The Wechsler Adult Intelligence Scale (WAIS) Digit Symbol Substitution and Copy Tests.—The WAIS Digit Symbol Substitution Test was used to measure visuomotor coordination and attention, while Digit Symbol Copy test was used to measure psychomotor speed (Lezak, 1995). First, participants were administered the substitution test. Participants were presented 9 digits paired with distinct symbols. Participants were given 90 seconds to write symbols that correspond to the digits in each box. The score consisted of the number of correctly written symbols, with higher scores indicating better visuomotor coordination. Similarly, the symbol copy test consisted of 93 symbols and participants were asked to copy the symbol in the adjacent boxes provided. The time it took for participants to complete the task was recorded with less time to complete the task indicating better psychomotor speed.

Useful Field of View (UFOV®).—This computerized test was used to measure visual attention and SOP. Like previous studies, this test consisted of three subtests beginning with easy tasks that became more complex. In subtest 1, a measure of simple SOP, an object (car/truck) was displayed in the center of the computer screen at various speeds between 17 and 500 milliseconds and participants were asked to identify which object (car/truck) was displayed. In subtest 2, a measure of divided attention, participants were presented an object in the center of the computer screen in addition to a car in one of eight peripheral visual fields. Participants were asked to identify the central object while simultaneously selecting the peripheral location of the car. In subtest 3, a measure of selective attention, participants were asked again to identify the central object and location of the car in one of eight peripheral fields; however, the task was more difficult because there were distractors surrounding the central object and the peripheral car. The computer automatically presented

the central object at a slower speed when participants answered test items incorrectly; in the same manner, participants were presented the central object at the faster speed when they answered test tasks correctly. Visual SOP was calculated using the total in milliseconds of all three subtests; fewer milliseconds indicated faster visual SOP. Test-retest reliability is quite high and ranges from 0.74 to 0.81 (Ball et al., 2007).

Statistical Analysis

Data were examined using SPSS 21. Linear regression was used to impute PSQI baseline global scores for two participants, one with and the other without HIV. Specifically, two participants had a single missing component of the baseline PSQI (sleep quality and sleep disturbance); therefore, the remaining components were used to estimate the missing component for these two participants. From this, baseline global PSQI scores were both calculated. Out of 80 cases, fourteen were excluded from this analysis: nine with missing posttest data (HIV-positive = 4; HIV-negative = 5), one practice participant, and four other participants in the HIV-positive sample (one with a stroke, two with schizophrenia, and one with a stroke and schizophrenia). The demographic and baseline SOP and sleep differences between adults with and without HIV were examined using independent samples *t*-test and chi-square analyses (see Table 1). ANOVAs and chi-square analyses were used to examine demographics, mean global PSQI scores at baseline, and mean scores on SOP measures at baseline between the four training groups: HIV-positive tDCS ($n = 17$), HIV-positive sham tDCS ($n = 16$), HIV-negative tDCS ($n = 17$), and HIV-negative sham tDCS ($n = 16$) (see Table 2). For Aim 1, separate ANCOVAs were used to examine change in pre-post mean scores for global PSQI and SOP measures (controlling for age, education, and mean baseline scores for PSQI and SOP measures) for all four groups (see Table 3). Specifically, main and interaction effects of independent variables (HIV status and training group) were examined. In this study, separate ANCOVAs for each SOP outcome measure was performed because each SOP measure examined a different aspect of SOP. The Letter and Pattern Comparison Test measured speed and attention, the Digit Symbol Substitution Test measured visuomotor coordination and attention, the Digit Copy Test measured psychomotor speed, and the UFOV measured visual attention and SOP. For Aim 2, Pearson-product-moment correlation analyses were performed to examine change scores for PSQI and SOP measures (see Table 4A and 4B). The change scores for PSQI and the SOP measures were calculated by subtracting the posttest score from the baseline score. Correlation analyses were conducted for adults with and without HIV and separated by training groups. Since this was a pilot study with a limited sample size, correcting for multiple comparisons was not conducted.

Results

Descriptives and Group Differences

The adults with HIV ($M_{age} = 55.82$, range = 51–71 years of age) were significantly younger than those without HIV ($M_{age} = 62.12$, range = 50–87 years of age). Compared to adults without HIV, there were significantly more racial minorities ($\chi^2[n = 28] = 5.99$), $p = .01$) and men ($\chi^2[n = 22] = 10.28$), $p < .01$) among those with HIV. Adults without HIV had a significantly higher income and were more educated than those with HIV ($p < .01$).

As seen in Table 1, for mean global PSQI scores, adults with HIV scored higher (M = 9.65; SD = 5.14) which indicated significantly poorer sleep quality compared to those without HIV at baseline (M = 5.23; SD = 3.24), $t(54) = 4.18$, $p < .01$, d = 1.03. For SOP measures, adults without HIV scored significantly better ($M_{number\ correct}$ = 31.91; SD = 6.90) on the Pattern Comparison Test compared to adults with HIV ($M_{number\ correct}$ = 28.36; SD = 6.25), $t(64) = 1.46$, $p < .15$, d = 0.54. Sleep and SOP differences were further examined across the four training groups. As seen in Table 2, there were significant differences ($p < .01$) in age, gender, race, education, household income, global PSQI scores, and Pattern Comparison scores among the four training groups at baseline. At baseline, the two groups of adults without HIV that received either tDCS with SOP training or sham tDCS with SOP training were older, had more income, were more educated, had lower global PSQI scores (better sleep quality), and scored better on the Pattern Comparison Test. Therefore, age, education, and baseline PSQI and SOP scores were controlled to reduce confounding effects.

Aim 1 - Examine changes in global sleep quality and SOP among older adults with and without HIV who received tDCS or sham tDCS with SOP training.

The mean number of adults with HIV and without HIV separately by training group at baseline and posttest are presented in Table 3, alongside an ANCOVA analysis of the effects of HIV status, tDCS, and their interaction on the post-measures (controlling for age, education, and baseline scores).

Changes in Global Sleep Quality Post-Training—After controlling for age, education, and baseline global PSQI scores, there were no significant differences in global sleep quality between the groups post-training (all p values > .05). Although not significant, the greatest change in sleep quality was detected among the HIV-positive sham tDCS with SOP group.

Changes in SOP Post-Training—After controlling for age, education, and baseline SOP scores, there were no significant differences in scores on the Pattern Comparison, Digit Substitution, and UFOV Tests between the groups post-training (all p values > .05). For the Digit Copy Test, a main effect for HIV ($F[1, 59] = 5.26$, $p = .03$, $\eta_p^2 = .082$) and a main effect for tDCS ($F[1, 59] = 5.16$, $p = .03$, $\eta_p^2 = .080$) were detected; those who had HIV and/or received sham tDCS with SOP training performed better on the Digit Copy Test. A HIV-by-tDCS interaction on the Letter Comparison Test was significant ($F[1, 59] = 5.50$, $p = .02$, $\eta_p^2 = .085$); follow up pairwise comparisons using least significant differences showed that among adults with HIV, those who received tDCS with SOP training scored significantly better than those who received sham tDCS with SOP training ($p = .019$), while there was no significant difference by condition among those without HIV ($p = .244$). Scores on the UFOV improved across all the groups ($F[1, 59] = 64.76$, $p < .001$, $\eta_p^2 = .523$); however, there were no significant main effects for HIV ($F[1, 59] = 1.82$, $p = .18$) and tDCS ($F[1, 59] = .01$, $p = .94$) detected. This finding is consistent with previous studies of SOP training (without tDCS) in adults with and without HIV (Ball et al., 2007; Vance et al., 2012).

Aim 2 – Examine correlations between change scores for global PSQI and SOP measures by training group.

As seen in Table 4A and 4B, correlations between change scores for global PSQI and SOP measures were examined by HIV status and training groups. For adults without HIV who received sham tDCS with SOP training, change score for global PSQI was significantly correlated with change score for UFOV ($r = -.670$; $p < .01$); from baseline to posttest, improvements on PSQI correlated to declines (i.e., faster speed) on UFOV. For adults with HIV who received sham tDCS with SOP training, change score for global PSQI was significantly correlated with change score for Digit Symbol Substitution ($r = -.619$; $p < .01$); from baseline to posttest, improvements on PSQI correlated to improvements on Digit Symbol Substitution. For adults with and without HIV receiving tDCS with SOP training, there were no significant correlations between change scores for global PSQI and SOP measures.

Discussion

Findings from this study were consistent with those from previous studies in that older adults with HIV have poorer sleep quality compared to those without HIV (Vance & Burrage, 2005). For Aim 1, no significant improvements in global sleep quality were detected across the groups. This finding was not surprising for this pilot study with such a small sample size. Significant improvements on the Letter Comparison Test were observed post-training for the HIV-positive tDCS with SOP training group. Contrary to our hypotheses, significant improvements on the Digit Copy Test were observed post-training for the HIV-positive and HIV-negative sham tDCS with SOP training groups. It was possible the combined interventions counteracted each other despite their documented independent effects on sleep and cognitive function. The independent effects of tDCS on the outcome variables could not be examined as all the groups received SOP training, and thus there was no tDCS only condition. As expected, scores on the UFOV improved across all groups which provides further evidence that SOP training can improve SOP abilities in older adults with HIV, and possibly those with HAND. However, again we did not have a pure control group to compare the SOP training against.

Furthermore, for Aim 2, significant correlations between change scores for global PSQI and SOP measures (i.e., UFOV and Digit Symbol Substitution) were detected. For the HIV-negative sham tDCS with SOP training group, improvements on global PSQI correlated with better performance on UFOV. Similarly, for the HIV-positive sham tDCS with SOP training group, improvements on global PSQI correlated to improvements on Digit Symbol. Perhaps, the PSQI may not have been sensitive enough in this study to detect subtle changes in sleep quality. Various components of sleep can be better examined using actigraphy. Although costly, polysomnography should be considered for future study of tDCS and SOP training in adults with HIV with severe insomnia.

Strengths and Limitations

In this study, three strengths were obvious. First, this study provided an excellent opportunity to compare an intervention in two different, but related, populations. Second,

because stratified randomization was used to assign adults with and without HIV to the training groups, there was minimal sampling bias. Finally, this was the first study to examine the application of tDCS aimed at improving sleep in the context of a cognitive intervention.

Additionally, there were six limitations in this study. First, imputed data could potentially influence the results and limit generalizability; however, as this was conducted for 2 cases only, the possible bias was minimal (Schafer, 1999). Second, PSQI is a subjective measure of sleep quality, and participants may have under or over reported their sleeping problems. While the PSQI was used to inquire about sleep patterns over the past month, the 5 weeks in which participants were training also overlapped when participants commented about their sleep quality at posttest. Thus, the full treatment had not been delivered by the time participants rated their sleep quality. The training effects on sleep quality may have been attenuated. In this study, this measure of sleep quality was used to examine differences between adults with and without HIV; however, some components of the PSQI (e.g., number of hours of sleep per night) were not examined. Third, although participants were asked about cognitive impairment during telephone screening, there was lack of objective data for neurocognitive performance. Fourth, statistical power was reduced due to the small sample sizes. Unfortunately, conducting an intervention study of this intensity is costly, thus preventing recruitment of larger samples. Larger sample sizes and longitudinal studies are needed to detect true differences across training groups in global sleep quality and SOP. Fifth, there was no correction for multiple comparisons due to this study being a pilot study. In this pilot study, scores on the SOP measures were analyzed separately with more specificity than as a global score. Finally, this study lacked a non-SOP comparative group which limited generalizability of these results.

Implications for Practice

Granted that SOP training did not improve sleep, it has consistently shown to improve SOP in adults with and without HIV (Ball et al., 2007; Vance, Fazeli, Ross, Wadley, & Ball, 2012). Independently, SOP training can improve cognitive function and other cognitive influences such as depression which may indirectly improve sleep over time. Also, for clinicians caring for adults with HIV, it is important to perform thorough assessments focusing on factors that influence sleep especially for those with cognitive impairments. Routine sleep assessments in the clinical setting can help provide insight on other health issues that can affect cognitive functioning such as depression (Gamaldo et al., 2013) and sleep apnea (Yaffe et al., 2014). In fact, early diagnosis and treatment of sleep problems can improve cognitive functioning which may also help adults aging with HIV remain independent in their everyday functioning activities (e.g., taking medications).

Implications for Research

With the increasing number of adults aging with HIV, more research is needed to identify ways to address problems such as poor sleep given its negative affect on cognitive functioning (Vance, Heaton, Eaves, & Fazeli, 2011). Although there are lack of studies showing the impact of tDCS on sleep, future objectives should focus on the mechanisms in which cortical stimulation can improve sleep quality. Further exploration of variations in tDCS application and techniques, montage, number of training sessions, and frequency of

exposure are needed to examine its modulating effects on sleep disorders such as insomnia. Although the groups in this study did have PSQI scores above clinical cutoffs, future studies should examine the effects of cognitive training and tDCS only among adults with HIV with severe insomnia.

While this article focused on tDCS, recent evidence has shown that newer modalities of transcranial direct current stimulation such as transcranial alternating stimulation current stimulation (tACS) can be beneficial for stimulating cortical excitability (Inukai et al., 2016). In tACS, during half of the cycle, one electrode serves as the anode and the other as the cathode at a lower current. During the other half of the cycle, the pattern reverse and the former anode now serves as the cathode and vice versa. Hence, tACS may influence brain oscillations which can also improve sleep (Vance, Fazeli, Cody, Bell & Pope, 2016). Such methods necessitate further examination of its applicability and modulatory effects on sleep-related cognitive functions in older adults with HIV, particularly those at risk for HAND.

Conclusion

While the application of transcranial electrical devices in conjunction with other cognitive training programs and treatments may improve health outcomes in many populations, further exploration of various techniques is needed to ensure proper usage and safety. Accurate application to specific brain areas is necessary as well as close monitoring for long-term effects. As this area of study continues to develop, a greater focus on cognitive training in addition to lifestyle behaviors such as sleep hygiene may be beneficial for adults with HIV as they age.

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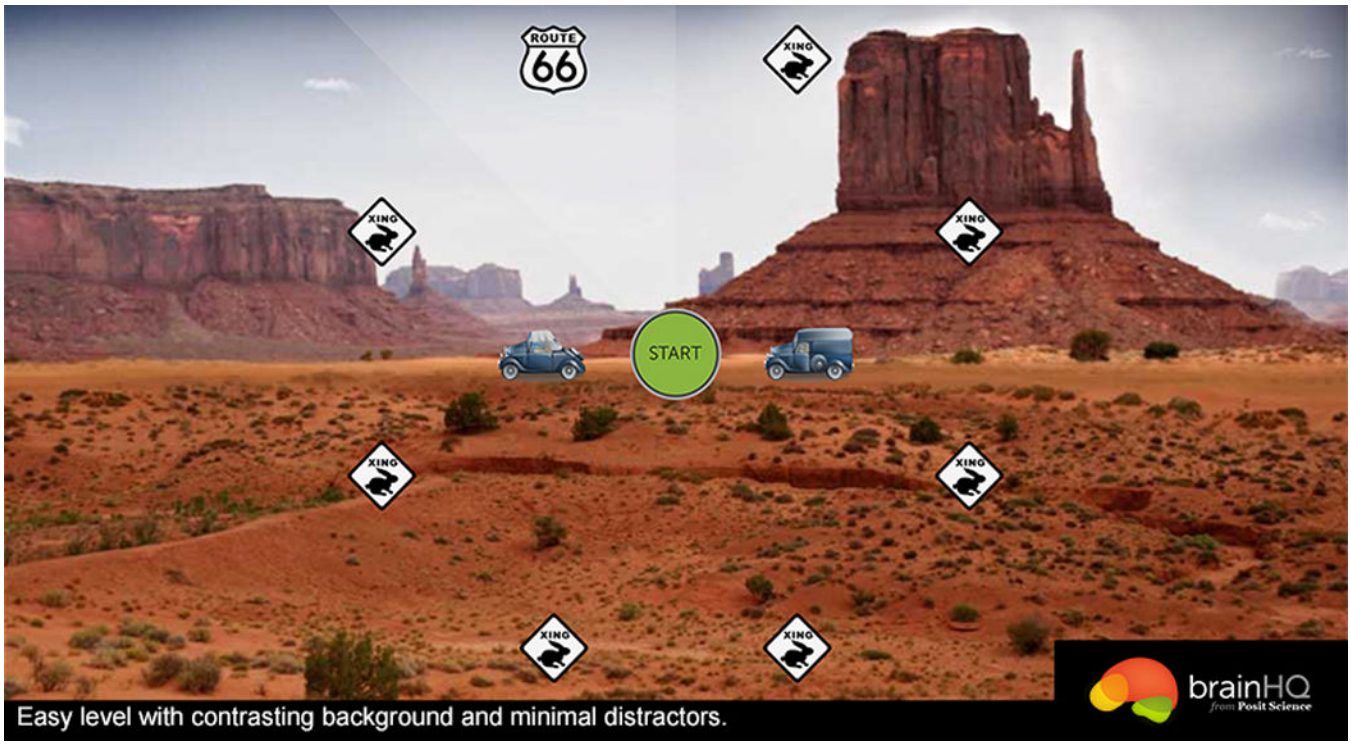

Figure 1.
Double Decision task (BrainHQ) involves identifying a central object (car/truck) and ther peripheral location of the Route 66 sign.

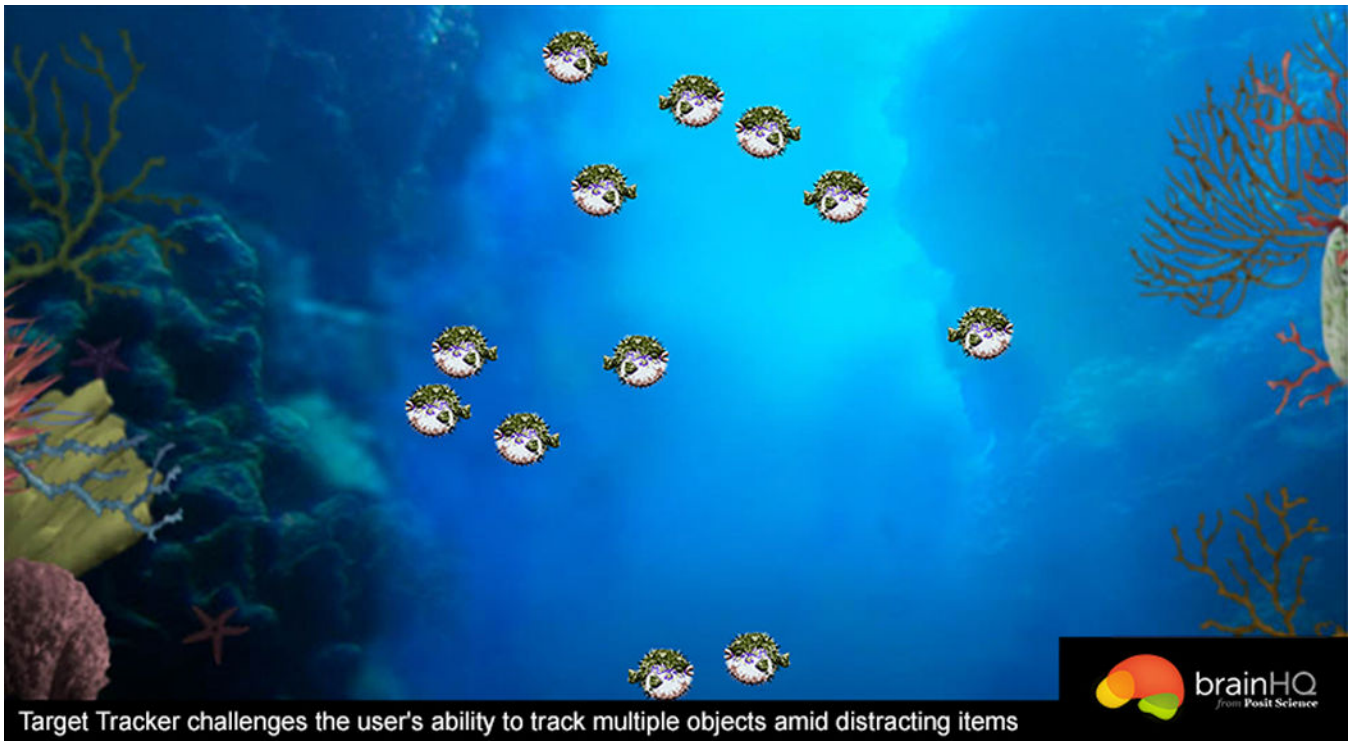

Figure 2.
Target Tracker (BrainHQ) task involves identifying the original locations of balls/jellyfish.

Table 1.

Baseline Demographic, Sleep, and SOP Differences Between Groups by HIV-Status

Variable	HIV-Positive (*n* = 33)		HIV-Negative (*n* = 33)		
	M (*SD*)	*N* (%)	*M* (*SD*)	*N* (%)	*p*
Age	55.82 (4.34)		62.12 (10.40)		.00**
Gender					.00**
Women		11 (33%)		24 (73%)	
Men		22 (67%)		9 (27%)	
Race					.01**
Minority		28 (85%)		19 (58%)	
Nonminority		5 (15%)		14 (42%)	
Household Income†	1.67 (.645)		4.95 (2.89)		.00**
Education (years)	12.58 (1.86)		14.88 (1.85)		.00**
Letter Comparison (no. correct)	40.15 (9.70)		43.79 (10.52)		.15
Pattern Comparison (no. correct)	28.36 (6.25)		31.91 (6.90)		.03*
Digit Symbol Substitution (no. correct)	40.55 (12.81)		46.39 (15.11)		.10
Digit Copy Test (seconds)	97.33 (30.21)		86.93 (24.67)		.13
Useful Field of View (milliseconds)	427.54 (248.64)		471.70 (248.42)		.47
Global Pittsburgh Quality Sleep Index	9.65 (5.14)		5.23 (3.24)		.00**

Note. *M* = mean; *SD* = standard deviation; SOP = speed of processing; no = number; tDCS = transcranial direct current stimulation

† = (1 = $0-$10,000; 8 = more than $70,000)

* $p \leq .05$

** $p \leq .01$

Table 2.

Demographic, Sleep, and SOP Differences Between Training Groups at Baseline Using ANOVA and Chi-square Analyses ($N = 66$)

	HIV-Positive tDCS + SOP ($n = 17$)		HIV-Positive sham tDCS + SOP ($n = 16$)		HIV-Negative tDCS + SOP ($n = 17$)		HIV-Negative sham tDCS + SOP ($n = 16$)		
Variable	***M* (*SD*)**	***N* (%)**	***M* (*SD*)**	***N* (%)**	***M* (*SD*)**	***N* (%)**	***M* (*SD*)**	***N* (%)**	**p-value**
Age (years)	56.00 (3.24)		55.63 (5.38)		62.65 (11.03)		61.56 (10.01)		.00 **
Gender									
Women		6 (35.3%)		5 (31.3%)		13 (76.5%)		11 (68.8%)	.00 **
Men		11 (64.7%)		11 (68.8%)		4 (23.5%)		5 (31.3%)	
Race/Ethnicity									
Minority		14 (82.4%)		14 (82.4%)		13 (76.5%)		7 (43.8%)	.01 **
Nonminority		3 (17.6%)		2 (17.6%)		5 (23.5%)		9 (56.2%)	
Education (years)	12.53 (1.77)		12.63 (2.00)		15.05 (2.09)		14.84 (1.91)		.00 **
Household Income †	1.71 (.69)		1.63 (.62)		4.47 (3.04)		5.31 (2.85)		.00 **
Global PSQI	9.88 (6.10)		9.44 (4.37)		5.41 (3.81)		5.13 (2.67)		.00 **
Letter Comparison	38.82 (10.79)		41.56 (8.50)		44.47 (11.61)		43.06 (9.56)		.17
Pattern Comparison	28.24 (6.91)		28.50 (5.70)		31.24 (6.43)		32.63 (7.51)		.03 *
Digit Symbol	39.00 (11.88)		42.19 (13.93)		45.47 (15.28)		47.38 (15.38)		.07
Digit Copy Test	98.64 (31.17)		95.95 (30.11)		88.40 (21.92)		85.37 (27.96)		.14
Useful Field of View	427.68 (278.58)		427.40 (221.59)		479.53 (272.09)		463.38 (229.21)		.48

Note. *M* = mean; *SD* = standard deviation; SOP = speed of processing; tDCS = transcranial direct current stimulation; standard deviation; SOP SOP = speed of processing; tDCS = transcranial direct current stimulation; Pittsburgh Sleep Quality Index

† = (1 = $0-$10,000; 8 = more than $ than 70,000)

* $p \leq .05$

** $p < .01$

Table 3.

Change Scores for Sleep Quality and SOP Measures and ANCOVA Results of HIV, tDCS, and HIV x tDCS Interaction Controlling for Age, Education, and Baseline Scores

	HIV-Negative		**HIV-Positive**		**ANCOVA on Post-tDCS, Controlling for Age, Education and Baseline Scores**							
	sham tDCS + SOP *n* = 16	**tDCS + SOP *n* = 17**	**sham tDCS + SOP *n* = 16**	**tDCS + SOP *n* = 17**		**HIV Status**		**tDCS**		**HIV Status x tDCS**		
	M	*M*	*M*	*M*	Error *df*	*F* (1, *df*)	*p*	*F* (1, *df*)	*p*	*F* (1, *df*)	*p*	R^2
Global PSQI	1.44	0.29	9.44	1.38	59	1.28	.263	1.89	.174	.266	.608	.710
Letter Comparison $^{H\ x\ t}$	1.38	0.18	0.18	4.47	59	.022	.882	1.661	.203	5.501	.022	.796
Pattern Comparison	0.07	0.52	2.81	1.58	59	1.095	.300	.267	.608	.873	.354	.781
Digit Symbol Substitution	4.75	0.94	4.12	4.06	59	.152	.698	3.484	.067	2.183	.145	.888
Digit Copy $^{H,\ t}$	3.77	0.52	15.16	6.32	59	5.257	.025	5.163	.027	.547	.463	.812
Useful Field of View	184.07	191.76	133.33	131.85	59	1.824	.182	.006	.940	.011	.917	.572

Note. *M* = mean, SOP = speed of processing; tDCS = transcranial direct current stimulation; PSQI = Pittsburgh Sleep Quality Index; HIV-by-tDCS interaction = $^{H\ x\ t}$; HIV main effect = ^{H}, tDCS main effect = ^{t}; *p* significant at .05

Table 4a.

Bivariate Correlations of Change Scores for Global PSQI and SOP for HIV-Negative Adults by Training Group

		Global PSQI	Letter Comparison	Pattern Comparison	Digit Symbol Substitution	Digit Copy Test	Useful Field of View
sham tDCS + SOP	Global Pittsburgh Quality Sleep Index	-					
	Letter Comparison (no. correct)	−.157	-				
	Pattern Comparison (no. correct)	−.261	.017	-			
	Digit Symbol Substitution (no. correct)	−.289	.363	−.191	-		
	Digit Copy Test (seconds)	.179	−.151	.299	−.413	-	
	Useful Field of View (milliseconds)	−.670**	−.150	.219	-.092	.200	-
tDCS + SOP	Global Pittsburgh Quality Sleep Index	-					
	Letter Comparison (no. correct)	-.204	-				
	Pattern Comparison (no. correct)	.133	.606**	-			
	Digit Symbol Substitution (no. correct)	.120	.141	.301	-		
	Digit Copy Test (seconds)	.097	−.353	−.667**	−.373	-	
	Useful Field of View (milliseconds)	−.150	.554*	.289	−.210	.045	-

Note.

*$p < .05$

**$p < .01$.

Correlations indicate the relationship between the change in Global Pittsburgh Quality Sleep Index score and speed of processing measures by intervention group from baseline to posttest.

Table 4b.

Bivariate Correlations of Change Scores for Global PSQI and SOP for HIV-Positive Adults by Training Group

		Global PSQI	Letter Comparison	Pattern Comparison	Digit Symbol Substitution	Digit Copy Test	Useful Field of View
sham tDCS + SOP	Global Pittsburgh Quality Sleep Index	-					
	Letter Comparison (no. correct)	−.442	-				
	Pattern Comparison (no. correct)	−.183	.388	-			
	Digit Symbol Substitution (no. correct)	−.619*	.103	.429	-		
	Digit Copy Test (seconds)	.034	−.131	−.501*	−.403	-	
	Useful Field of View (milliseconds)	.087	−.157	−.526*	−.197	.063	-
tDCS + SOP	Global Pittsburgh Quality Sleep Index	-					
	Letter Comparison (no. correct)	−.213	-				
	Pattern Comparison (no. correct)	.004	.539*	-			
	Digit Symbol Substitution (no. correct)	.003	.060	.164	-		
	Digit Copy Test (seconds)	−.222	−.343	−.307	.011	-	
	Useful Field of View (milliseconds)	−.094	.481	.136	.154	−.387	-

Note.

*$p < .05$

**$p < .01$.

Correlations indicate the relationship between the change in Global Pittsburgh Quality Sleep Index score and speed of processing measures by intervention group from baseline to posttest.