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A pilot investigation on the effects of combination transcranial direct current stimulation and speed of processing cognitive remediation therapy on simulated driving behavior in older adults with HIV.

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Abstract

Cognitive impairments seen in people living with HIV (PLWH) are associated with difficulties in everyday functioning, specifically driving. This study utilized speed of processing cognitive remediation therapy (SOP-CRT) with transcranial direct current stimulation (tDCS) to gauge the feasibility and impact on simulated driving. Thirty PLWH (M_{age} = 54.53, SD = 3.33) were randomly assigned to either: sham tDCS SOP-CRT or active tDCS SOP-CRT. Seven indicators of simulated driving performance and safety were obtained. Repeated measures ANOVAs controlling for driver's license status (valid and current license or expired/no license) revealed a large training effect on average driving speed. Participants who received active tDCS SOP-CRT showed a slower average driving speed (p = 0.020, d = 0.972) than those who received sham tDCS SOP-CRT. Non-significant small-to-medium effects were seen for driving violations, collisions, variability in lane positioning, and lane deviations. Combination tDCS SOP-CRT was found to increase indices of cautionary simulated driving behavior. Findings reveal a potential avenue of intervention and rehabilitation for improving driving safety among vulnerable at-risk populations, such as those aging with chronic disease.

Keywords

driving; HIV/AIDS; cognitive remediation therapy; Brain simulation; neuromodulation; tDCS

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1. Introduction

1.1. HIV, aging, and mobility

By the year 2020, 70% of the individuals currently living with HIV are expected to be 50 years old and older (High et al., 2012) due to medical advances such as combination antiretroviral therapy (cART) and better knowledge and care for the disease (Sheppard et al., 2017). Declines normally associated with the aging process are accompanied with deficits in cognition, including processing speed, or the rate at which an individual processes and uses information from the environment (Glisky, 2007). With HIV, the discussion of premature aging is of interest as studies show evidence of both age-related deficits at younger ages (i.e., accelerated aging) and exacerbated age-related deficits in age-normative declines (i.e., accentuated aging; Sheppard et al., 2017). Furthermore Greene et al. (2015) found that people living with HIV (PLWH) aged 50 and older reported high rates of geriatric syndromes (e.g., diseases, problems, frailty, or syndromes normally associated with aging), including impairments with mobility, cognition, and difficulties with instrumental activities of daily living (IADL).

1.2. Driving Rehabilitation

One common IADL, rated high in importance for older adults, is driving. Driving is a complex task that involves multiple cognitive, behavioral, and environmental factors (Anstey, Wood, Lord, & Walker, 2005; Pope, Bell, & Stavrinos, 2017; Pope, Ross, & Stavrinos, 2016). Driving cessation has been associated with a multitude of negative health outcomes including decreased engagement in social activities (Marottoli et al., 2000), poorer psychological well-being including higher ratings of depression and lower life satisfaction (Siren, Hakamies-Blomqvist, & Lindeman, 2004), and declines in physical functioning (Edwards, Lunsman, Perkins, Rebok, & Roth, 2009). Prior research has focused heavily on clinical populations such as those living with traumatic brain injury (TBI; Ortoleva, Brugger, Van der Linden, & Walder, 2012), dementia (Reger et al., 2004), and HIV (Marcotte et al., 1999) as they have shown driving performance deficits that vary with disease severity when compared to healthy controls. Specifically, for PLWH who had cognitive impairment, higher failure rates on simulated driving scenarios, more simulated driving collisions, and higher likelihood of being rated as unsafe on driving evaluation scores were seen when compared to those with HIV who did not show cognitive impairment (Marcotte et al., 1999; Marcotte et al., 2006; Marcotte et al., 2004). Furthermore, a pilot study by Vance, Fazeli, Ball, Slater, and Ross (2014) also found a significant association between various HIV related variables (CD4 count), self-reported driving history (days driven per week), simulated driving performance (reaction time, speeding, divided attention), and cognitive performance (speed of processing [SOP], attention, memory, cognitive flexibility) adding to the multifactorial processes linked with driving.

Studies investigating the neural mechanisms underlying driving behavior and performance suggest activation of multiple brain areas such as the pre-motor, cerebellar, and frontoparietal areas (Graydon et al., 2004; Spiers & Maguire, 2007), depending on the driving behavior or task at hand. One such area includes the ventral attention system, which encompasses the temporoparietal junction and the ventral frontal cortex (Fox, Corbetta, Snyder, Vincent, & Raichle, 2006; Vossel, Geng, & Fink, 2014) and is associated with the salience network (Sridharan, Levitin, & Menon, 2008). Neural activation corresponds to unexpected stimuli which diverts or cues resources away from the focus of spatial attention (Vossel et al., 2014). Spiers and Maguire (2007) found neural evidence suggesting the activation or role of the ventral frontal cortex during various driving maneuvres such as turning and stopping. These findings add support for the investigation into rehabilitative interventions that include the cognitive processes related to driving such as SOP, attention, and cognitive control.

1.2.1. Speed of processing cognitive remediation therapy (SOP-CRT)—An innovative and frequently studied form of driving rehabilitation is speed of processing cognitive remediation therapy (SOP-CRT; Ball, Edwards, & Ross, 2007; Ball, Edwards, Ross, & McGwin, 2010; Edwards, Myers, et al., 2009; Roenker, Cissell, Ball, Wadley, & Edwards, 2003). This type of CRT utilizes a paradigm of visual SOP and attentional control processes to target processing speed abilities (Ball et al., 2007). Individuals who received 10 sessions of SOP-CRT in the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) clinical trial (Ball et al., 2002) showed SOP training gains which were maintained over 2 years and lower rates of at-fault motor vehicle collisions (MVCs) 6 years after the initial training (Ball et al., 2010). Furthermore, Vance, Fazeli, Ross, Wadley, and Ball (2012) found that SOP-CRT in PLWH was associated with better SOP and performance on a timed IADL task at post-test when compared to the no-contact control group.

1.2.2. Non-invasive brain simulation – Transcranial direct current stimulation (tDCS)—Non-invasive brain stimulation via transcranial direct current stimulation (tDCS) is a safe, common, and widely studied neuro-modulation technique (Ahn et al., 2017; Bikson et al., 2016; Fazeli, Woods, Pope, Vance, & Ball, 2017; Nitsche & Paulus, 2000; Priori, Berardelli, Rona, Accornero, & Manfredi, 1998; Szymkowicz , McLaren, Suryadevara, & Woods, 2016; Woods et al., 2016; Woods et al., 2014). tDCS is thought to modulate cortical neuronal membrane potentials which may alter cortical activity such as spontaneous neuronal activity or changes in neurotransmitters (Woods et al., 2016). Sub-threshold stimulation is administered to the scalp, targeting relevant cortical areas and neuronal networks, yet when using conventional electrodes (in contrast to high-definition) focality is limited and widespread effects are expected (Kessler et al., 2013; Minhas et al., 2010; Minhas, Bikson, Woods, Rosen, & Kessler, 2012; Woods et al., 2016). Membrane polarization and observed behavioral effects are conditional to whether stimulation is anodal (positive charge) or cathodal (negative charge) and the specific tDCS placement (i.e., montage) used (Scheldrup et al., 2014; Woods et al., 2016).

The behavioral findings regarding tDCS on cognitive and motor task outcomes are mixed, with effect sizes depending on methodological design and tDCS factors such as polarity and selected montages (Hsu, Ku, Zanto, & Gazzaley, 2015; Jacobson, Koslowsky, & Lavidor, 2012; Nilsson, Lebedev, Rydström, & Lövdén). Less investigated, is the role of tDCS with complex, real-world behavior such as driving (Scheldrup et al., 2014). Beeli, Koeneke, Gasser, and Jancke (2008) showed immediate change in simulated driving performance, with individuals who received 15 minutes (min) of 1 milliamp (mA) anodal tDCS stimulation to the left and right dorsolateral prefrontal cortex (DLPFC; 10–20 international system: F3 and F4, respectively) with the cathode placed on the ipsilateral mastoid, exhibiting overall more cautionary driving behavior (i.e., larger headway distances, fewer speed violations, slower driving speed, and fewer revolutions per minute). Similar findings were found by Sakai, Uchiyama, Tanaka, Sugawara, and Sadato (2014) who showed better driving performance (e.g., longer headway distance and better lane keeping ability) when the tDCS anode was placed over F4 and the cathode over F3 compared to the cathode over F4 and anode over F3 as well as the sham stimulation.

1.2.3. Combination tDCS and CRT—While the exact mechanism behind the alteration in neuronal activity is still unknown, combination tDCS and CRT has been a recent popular methodological design regarding behavior change (Vance, Fazeli, Cody, Bell, & Pope, 2016). While debated, it has been hypothesized that larger or heightened CRT or learning effects will be observed in the presence of tDCS, as both have independently shown evidence of neuroplasticity in healthy and clinical populations (Hill, Fitzgerald, & Hoy, 2016; Nilsson, Lebedev, Rydstrom, & Lovden, 2017; O'Brien, Lister, Peronto, & Edwards, 2015; Scheldrup et al., 2014; Takeuchi & Kawashima, 2012; Woods et al., 2016).

Regarding complex, real-world behavior, Clark et al. (2012) found that when 2.0 mA tDCS stimulation with the anode over the right inferior frontal cortex (rIFC; 10–20 international system: F10) and the cathode placed on the contralateral shoulder was paired with virtual threat-identification training, immediate accuracy of identifying concealed objects was improved compared to those receiving sham stimulation or 2mA stimulation with the anode over the partial cortex. This combination paradigm was extended to airplane pilot training, which found limited behavioral learning evidence, but significant changes in neural activity of the DLPFC and primary motor cortex (Choe, Coffman, Bergstedt, Ziegler, & Phillips, 2016). In HIV-positive populations specifically, there are currently two studies investigating combination tDCS and CRT. Ownby and Acevedo (2016) utilized a racing video game (albeit, not a true CRT) in conjunction with 20 minutes of 1.5 mA tDCS with the anode over F3 and the cathode placed over the right supraorbital area. Similarly, Fazeli et al. (2017), the parent study of the current sample and procedure investigated, utilized an online SOP-CRT, Brain HQ (Posit Science) with the same montage as Clark et al. (2012) (anode over F10 and the cathode on contralateral shoulder). Both studies found medium-to-large effect sizes related to training group by time interactions, but limited statistical training-related change conceivably due to small sample sizes and lack of no-contact control groups. Regarding driving, while cognitive training and driving simulator training in isolation has been investigated in samples of older adults (Casutt, Martin, Keller, & Jäncke, 2014; Cuenen, Jongen, Brijs, Brijs, Houben, et al., 2016; Cuenen, Jongen, Brijs, Brijs, Lutin, et al., 2016), it is yet to be tested whether combination tDCS and CRT would generalize to real-world behavior and significantly affect simulated driving performance.

1.3. Specific aims and hypotheses

The overall aim of the pilot study was to preliminarily investigate the feasibility and effects of combination tDCS SOP-CRT on driving simulator outcomes in individuals aged 50 and older living with HIV. The current study utilized data from the aforementioned Fazeli et al., 2017 study; this parent study examined neurocognitive outcomes of tDCS SOP-CRT while the current study examines driving simulator outcomes. This study extends the limited existing literature on combination tDCS SOP-CRT findings in PLWH by examining this training paradigm on an important everyday functioning outcome. It was hypothesized that individuals who received the active tDCS SOP-CRT would show more cautionary driving behavior (i.e., reduction in overall driving deviations, violations, collisions, less variability in lane positioning, faster reaction time to hazards, slower speed, and less speed variability) at post-test when compared to the sham tDCS SOP-CRT group.

2. Method

2.1. Participants

Adults 50 and older, all who were HIV-positive and from the Birmingham-metro area, were recruited via Institutional Review Board approved flyers at a university affiliated HIV clinic in the southeast.

All participants met the self-report inclusion criteria of: (1) being HIV-positive and a current patient at the university affiliated HIV clinic, (2) 50 and older, (3) having a stable address (e.g., not homeless), (4) being able to speak and understand English, (5) having no mental impairments (e.g., Alzheimer's disease, dementia, or mental retardation), (6) not being legally blind or deaf, (7) not currently undergoing radiation or chemotherapy, (8) no history of a brain trauma with loss of consciousness greater than 30 min, (9) no neurological problems (e.g., schizophrenia, bipolar disorder, migraines, history of stroke, epilepsy, or history of seizures), (10) not having untreated hypertension, (11) no intracranial metal plates, implants, or biomedical devices, and (12) being right-handed. Given that we wanted to examine the effect of the intervention on driving behaviors in both non-current drivers as well as current driver (regardless of whether one was a *licensed* driver or not), driver's license status was not included in the eligibility criteria. Further, as 23.3% ($n = 7$) of the final sample reported driving at least one day per week without a valid driver's license; this confirmed the importance of examining all classifications of drivers in this sample. In efforts to have a well representative sample, driving exposure (i.e., days driven per week and driver's license status) was assessed and used for further analyses. Furthermore, Blows, Ameratunga, Ivers, Lo, and Norton (2005) found that driving without a valid driver's license may indicate a higher level of risk for older drivers, putting them at a possible higher risk for MVCs.

In total, 119 individuals were screened, with 48 individuals meeting the self-report inclusion criteria and enrolled, of which 37 completed the baseline, training, and post-test visits (see Figure 1). After the clinic data were reconciled with self-report data after the completion of the study, it was determined that four of the 37 did not in fact meet inclusion criteria (clinic confirmed previous history of stroke and schizophrenia). These four participants were excluded from the main aim analyses reported in the parent study (Fazeli et al., 2017) given the potential effect of those conditions on cognitive functioning. The current study sample size differs from Fazeli et al. (2017) as it includes all participants who completed the simulated driving portion for baseline and post-test as well as the training. Given the exploratory nature of the described pilot study, this allowed us to maximize available simulator data to investigate the current research question. Of the 37 participants who completed all visits, four suffered from simulator sickness and were unable to complete the driving portion of the baseline and post-test visits, two failed the practice drive, and one participant did not complete the simulator portion of the post-test. Compared to the total sample, these seven individuals did not differ in demographic characteristics (p's > 0.05), except for on age ($t(38) = -2.27$, $p = 0.029$), with those without complete simulator data being older in age ($M_{years} = 58.14$, $SD = 6.52$) than those with complete simulator data ($M_{years} = 54.42$, $SD = 3.23$). The final sample consisted of 30 PLWH aged 50-63 years of age ($M_{age} = 54.53$, $SD = 3.33$). Of this sample (see Table 1), the majority were African American (86.7%), male (63.3%), and had a range of education from 9th grade to post-secondary education ($M_{years} = 12.40$, $SD = 1.85$).

2.2. Study procedure

Participants were screened via a 10-min telephone screener which included the inclusion criteria previously mentioned. If eligible, participants were scheduled for a 2-hour (h) baseline visit that involved informed consent, demographic intake, questionnaires, a comprehensive cognitive battery, and a drive in the driving simulator. After completion of the baseline visit, participants were randomly assigned (using a stratified randomization algorithm that matched the two groups on age, gender, years of education, and driving risk measured by the useful field of view [UFOV® task]), to a training group: sham tDCS SOP-CRT (referred to as the sham training group) or active tDCS SOP-CRT (referred to as the active training group). After group assignment, the participants were scheduled for 10 1-h training visits that were conducted in the lab by a trained researcher that was not affiliated with the baseline or post-test appointments, but was not blinded to the tDCS randomization. Post-test assessments were conducted by a blinded trained research assistant to minimize experimenter bias. These appointments were identical to baseline visits with the addition of an exit survey on sensations from the tDCS during training as well as expectancy effects of the training. Participants were compensated $50 for each baseline and post-test assessments, and $10 for each 1-h training sessions ($100), for a total of $200. This study was registered in ClinicalTrials.gov (NCT02391311) and has been further explained in more detail in Fazeli et al. (2017).

Both training groups received the same amount of SOP CRT (i.e., 10 1-h sessions). The tDCS electrode placement followed the unilateral monopolar montage provided in Clark et al. (2012) which targeted the ventral frontal cortex (anode over F10, cathode over the contralateral shoulder, 2mA, 20 minutes). Duration and stimulation strength was guided by empirical and clinical-based best practices and recommendations (Ahn et al., 2017; Bikson et al., 2016; Priori et al., 1998; Woods et al., 2016; Woods et al., 2014). The tDCS stimulation was administered with a Soterix conventional 1×1 device utilizing a single anode and cathode system and two saline soaked 5 cm by 7 cm sponges (4 ml per side of each sponge). A current of 2.0 mA was administered via the anode over F10 and cathode placed on the contralateral left shoulder. Cranial measurement and electrode placement was done before cognitive training began using the 10–20 international system. Stimulation was increased to 2.0 mA for all participants in the sham training group, remained at 2.0 mA for 30 seconds (s), and decreased back to 0, similar to other tDCS procedures (Nilsson et al., 2017). The active training group was administered stimulation at 2.0 mA for 20 consecutive min consecutively unless discomfort was reported at which the stimulation was decreased to a tolerable level. Various sensations related to the stimulation were assessed at 5 and 10-min marks of the simulation; see Fazeli et al. (2017). Participants in both conditions continued to wear the electrodes after the stimulation shut off at 20 min until after the 1-h training session was complete to prevent unintentional loss of blinding due to skin warming or redness occurring under the active electrodes vs. sham electrodes.

SOP-CRT was administered using BrainHQ (BrainHQ is a registered trademark of Posit Science, Inc., www.brainhq.com). Participants in both training groups were required to complete 10, 1-h training sessions alternating between Double Decision and Target Tracker, exercises designed to tap into visual attention and tracking speed (Edwards et al., 2015). Participants were instructed to complete the tasks that are presented in a gaming paradigm, allowing participants to see personal performance and gains. Ten, 1-h sessions, totaling to 10 h of training was chosen as it has shown efficacy in previous training paradigms (see Ball et al., 2002; Vance et al., 2012). Prior research demonstrates that pairing tDCS with training tasks simultaneously is more effective than delivering stimulation prior to training (Martin, Liu, Alonzo, Green, & Loo, 2014). Thus, both CRT and tDCS were delivered simultaneously. Further descriptive information on training parameters for the sample is presented in Table 1.

2.3. Measures

2.3.1. Demographics

Demographic Questionnaire.: A standard self-report questionnaire was given to participants at baseline to collect pertinent sociodemographic information such as age, gender, race, education, and health history. Along with general health history, self-reported length of diagnosis, current CD4 count, and viral load were obtained as well as clinic records to confirm self-reported health information.

Driving History Questionnaire.: A driving history questionnaire, administered in an interview style at baseline, was used to assess whether the participant possessed a current and valid driver's license. Participants also reported their current average amount of days driven per week (regardless of their driver's license status).

2.3.2. STISIM Driving Simulator (STISIM Drive, 2007)—Participants completed a practice drive (approximately 1 mile) and drove an experimental drive for approximately 5 miles (ranging from 10 – 15 minutes to complete depending on driving speed and reactions to hazards; Bishop, Biasini, & Stavrinos, 2017) in a driving simulator using STISIM drive technology (STISIM Drive, 2007). The standardized protocol was also previously used and published with a different clinical sample of drivers in Bishop et al. (2017). The simulation was displayed on three 20-inch LCD computer monitors. Participants sat within the simulator's driving compartment, which provided a view of the simulated roadway, rearview mirror, and dashboard instruments, which included a speedometer. Participants were instructed to move the steering wheel in a typical driving manner and to depress the accelerator and brake pedals accordingly. The simulator provided naturalistic engine sounds along with external road noise via the on-board stereo system. The participants were instructed to drive as they normally would on a real road and were monitored for driving simulator sickness in both the practice and experimental drives. If simulator sickness symptoms were apparent, the simulator drive was discontinued immediately. Participants drove alone in a room, without the experimenter visually present to reduce experimenter bias and external distraction.

The practice drive consisted of a two lane bi-directional road with suburban daytime scenery, similar to the experimental drive. To determine successful completion of the practice drive, participants had to successfully maneuver around an embedded hazard of a pedestrian walking out from behind a side-parked car. Successful completion of the practice drive consisted of completing the scenario without a collision within three successive tries. If a participant could not successfully complete the practice scenario within three successive tries, it resulted in exclusion from completing the experimental drive. The experimental drive consisted of a bi-directional roadway with simulated vehicles, cyclists, and pedestrians in both urban and suburban daytime scenery. The scenario contained 8 embedded hazards which were programmed to interact with the driver and elicit a behavioral response, such as releasing the accelerator, depressing the breaking, or swerving (Bishop et al., 2017). Based on previous hazard perception research, the hazards were categorized into three types: (1) behavioral prediction hazards (e.g., the hazard can be anticipated such as a car in clear sight on the side of the road that pulls into traffic), (2) environmental hazards (e.g., the hazard cannot be anticipated directly such as a child steps into the road from behind a van), and (3) dividing and focusing attention hazards (e.g., multiple hazard factors or precursors that the participant must monitor in the environment simultaneously such as busy intersections; Crundall et al., 2012). Scenario hazards varied between pedestrians, cyclists, and vehicles. To capture basic driving performance, the task demand was kept at a low level (e.g., no complex route planning or secondary distraction tasks). First reaction to the specific hazard along with other driving metrics and behaviors were recorded by the simulator.

Driving metrics: Lane deviations: the number of times the left tire of the vehicle came in contact with the center line or the right tire came in contact with the road edge (Stavrinos et al., 2015; Stavrinos et al., 2013).

Violations: the number of speed exceedances (the number of times the vehicle exceeds the speed limit by 8 mph or greater; Bishop et al., 2017), stop sign tickets, and traffic light tickets.

Collisions: the number of hit pedestrians, cyclists, objects, and simulated vehicles (number of times the simulated vehicle hit another vehicle in the scenario) as well as off-road collisions (number of times the simulated vehicle left the road past a predetermined distance threshold; Bishop et al., 2017; Stavrinos et al., 2015; Stavrinos et al., 2013).

Hazard reaction time (RT): time in s between the triggering of the hazardous event and one of four behavioral responses to all hazards (behavioral prediction, environmental, and focusing attention; Bishop et al., 2017). The behavioral responses included: 1) depressing the accelerator pedal by 10% to increase vehicle speed; 2) releasing the accelerator pedal by

10% to decrease vehicle speed (Rakauskas, Gugerty, & Ward, 2004; Stavrinos et al., 2015); 3) applying at least 1 pound of pressure to the brake pedal to decrease vehicle speed (Crundall, Andrews, van Loon, & Chapman, 2010; Garrison & Williams, 2013); and 4) moving the steering wheel by a 5-degree change to avoid hitting the hazard (Crundall et al., 2010; Garrison & Williams, 2013). Standard deviation of lane positioning (SDLP): lane positioning variability (i.e., swerving) in the section of the drive with no hazards (Marcotte et al., 2003; McGehee, Lee, Rizzo, Dawson, & Bateman, 2004; Stavrinos et al., 2015).

Average driving speed: average driving speed in miles per hour (mph) across the entire drive. Standard deviation (SD) of speed: speed variability or fluctuation in mph across the entire drive (Stavrinos et al., 2015; Stavrinos et al., 2013).

2.4. Data analyses

All analyses were conducted using IBM SPSS Statistics 23.0 (IBM Corp., 2014) and with an alpha value of 0.05.

2.4.1. Preliminary analyses—Shapiro-Wilk tests were conducted to assess the normality of the standardized residuals for all the simulated driving outcomes of interest between groups. Most of the driving outcomes between groups were non-normal (p's < 0.05). The data were not transformed in efforts of interpretation and that ANOVAs are generally robust to non-normality regarding Type I errors (Keselman et al., 1998), as well as the fact that this was a pilot study with the goal of examination of effect sizes of the intervention approach. Descriptive statistics as well as group differences on participant characteristics were conducted.

2.4.2. Repeated measures analysis of variance (RM-ANOVA) – Driving simulator outcomes—A series of separate two-way RM-ANOVAs were conducted to assess group mean differences in driving outcomes from pre-to post-test. For both models, training group (coded 0 = sham training group, 1 = active training group) was designated as the between-subjects factor and time (time point 1 = baseline, time point 2 = post-test) was designated as the within-subjects factor. In the second series of RM-ANOVA driver's license status (coded 0 = expired or no license, 1 = valid and current license) was added to the model to account for differences in driving per fo r ma nc e ba sed o n dr iver 's lice ns e st at us. Sensitivity analyses were conducted using analysis of covariance (ANCOVA) to account for individual differences in baseline performance and avoid interpreting possible regression to mean effects as training gains (Basak & O'Connell, 2016; Boot, Blakely, & Simons, 2011). Findings were similar across both tests; thus, RM-ANOVAs are reported below.

3. Results

Findings regarding tDCS sensations during training, perceptions regarding training, and combination tDCS SOP-CRT effects on cognitive outcomes (UFOV®, executive function, and language ability) is reported in the parent study (Fazeli et al., 2017). While not the aim of the current article, the time by training group interaction was tested for UFOV® in the current subsample (n = 30), and the same pattern was observed, a lack of significant time by training group interactions.

3.1. Preliminary results

As seen in Table 1, on average the sample drove 3.27 days per week (range = 0 – 7 days) and did not significantly differ between groups ($p = 0.084$). Over half of the sample reported having a valid and current driver's license ($n = 16$). There was a significant difference in the number of participants with a current driver's license and those who did not, ($p = 0.014$), with the active training group having more licensed drivers ($n = 11$) than the sham training group ($n = 5$). The two groups did not significantly differ on lab CD4 count ($p = 0.946$) and the majority ($n = 28$) reported an undetectable viral load. Given that current driver's license status significantly differed between the groups, all models were run controlling for driver's license status as well as days driven per week to investigate any possible influence on the training effect. Results were similar when conducted with either covariate, thus reported analyses controlled for driver's license status to account for group differences.

3.2. RM-ANOVAs – Driving simulator outcomes

Average driving simulator performance on the seven driving performance outcomes is listed in Table 2. When assessing unadjusted time and training group interactions for all the driving outcomes, training effects were found for average driving speed and lane deviations. At the alpha level of 0.05, average driving speed emerged as the only significant driving variable with a large effect, $F(1, 28) = 9.85$, $p = 0.004$, $\eta^2 = 0.260$, $d = 1.19$. Observation of the means seen in Figure 2a shows a 1.52 mph decrease in average driving speed for the active training group and a 2.74 mph increase in average driving speed for the sham training group. Regarding lane deviations, the time by group interaction was significant with a medium effect only at an alpha level of 0.10, $F(1, 28) = 3.57$, $p = 0.069$, $\eta^2 = 0.113$, $d = 0.714$. The same pattern was seen when observing the mean differences for lane deviations (see Figure 2b) as the active training group showed a decrease in lane deviations by 2.40 deviations while the sham training group increased in lane deviations by 1 deviation from baseline to post-test.

The interaction effect was not significant for driving violations ($p = 0.520$, $\eta^2 = 0.015$, $d = 0.247$), collisions ($p = 0.893$, $\eta^2 = 0.001$, $d = 0.063$), hazard RT ($p = 0.467$, $\eta^2 = 0.019$, $d = 0.278$), SDLP ($p = 0.719$, $\eta^2 = 0.005$, $d = 0.142$), and SD of speed ($p = 0.279$, $\eta^2 = 0.042$, $d = 0.419$). When investigating raw mean differences regardless of significance level from baseline to post-test, driving violations, hazard RT, and SD of speed showed the same pattern of change with the active training group showing 1.47 fewer violations, a 0.10 s faster RT, and a 0.23 mph smaller deviation in speed compared to the sham training group which showed 1.53 more violations, a 0.03 s slower RT, and a 0.67 mph larger deviation in speed. Driving collisions and SDLP showed a different pattern of change as both training groups showed fewer driving collisions (sham = 0.40, active = 0.33) and more deviation in lane positioning (sham = −0.14, active = −0.08) at post-test. The main effect of time was not significant for any of the driving outcomes (p's > 0.05), suggesting a lack of exposure or learning effect related to the driving simulator from baseline to post-test.

When controlling for current driver's license status (see Table 3), the significant large training effect for average driving speed was still evident ($d = 0.972$). The training effect at alpha level 0.10 was no longer present for lane deviations, yet the finding still revealed a medium effect in the direction as seen in the previous model (d = 0.640). No significant findings were found for any of the other simulated driving outcomes, but the effect sizes were similar in that small effects were seen for violations (d = 0.286) and collisions (d = 0.398). Interestingly, after controlling for driver's license status, the effect size improved for SDLP from no effect to a small sized effect (d = 0.514). No effect was seen for hazard RT (d = 0.063) and SD of speed (d = 0.090). When assessing the time by driver's license interaction, a significant large effect was present for SDLP (d = 0.876) and a medium effect at alpha level 0.10 for SD of speed (d = 0.756).

4. Discussion

Utilizing a combination tDCS and CRT methodological design, active tDCS SOP-CRT was found to affect certain, but not all, simulated driving behaviors as compared to sham tDCS SOP-CRT in older PLWH. Results suggested more cautionary driving behavior following active tDCS SOP-CRT as individuals randomized to that training group showed fewer lane deviations (number of centerline crossing and road edge excursions) and a slower average driving speed. These findings are in comparison to the sham training group who showed an increase in driving deviations and average driving speed. While not significant, inspection of raw mean differences revealed the same pattern of change with no-to-small effects sizes for driving violations (number of speed exceedances, stop sign tickets, and traffic light tickets), hazard RT (average of the first reaction time to behavioral prediction, environmental, and focusing attention hazards), and SD of speed.

After controlling for current driver's licensure status, the significant training effect was only evident for average driving speed. While lane deviations were no longer significant at an alpha level of 0.05 or 0.10, the same raw mean difference was evident with the active tDCS SOP-CRT group showing fewer lane deviations while the sham tDCS SOP-CRT group increased. Furthermore, while the p-value was no longer significant at an alpha level of 0.10, a medium effect was still present for lane deviations. This finding of a medium effect as well as the small effects found for SDLP, violations, and collisions with no statistical significance may be due to the relation between sample size and p-values, but not effect size (Sullivan & Feinn, 2012).

While cautionary or safer driving behavior should be interpreted with discretion, typical driving simulator safety studies focus on performance variables such as deviations and average speed, as indicators of driving safety (Wang, Zhang, Wu, & Guo, 2007). Regarding the current findings, the task at hand was for participants to drive as they normally would in an urban/suburban scenario which was embedded with unexpected hazards, potentially making slower speeds safer when avoiding such hazards. While slower driving speed may not always suggest safer driving (Horberry et al., 2004), studies have shown that faster driving speed is related to crash involvement (Aarts & van Schagen, 2006), such that faster speeds are related to increased crash risk (Aarts & van Schagen, 2006; Elander, West, & French, 1993). Furthermore, after administering anodal tDCS to DLPFC, Beeli et al. (2008) also found reductions in average speed, revolutions per minute (i.e., how many times the engine is turning per minute) and number of speed errors, and an increase in headway distance, suggesting a possible upregulation of safe driving behaviors. Regarding lane deviations, the findings may also conclude safer driving as increased lane deviations have shown association to distracted driving behaviors (Stavrinos et al., 2015; Stavrinos et al., 2013), which further increase crash risk and negative driving outcomes (Klauer et al., 2014; Stavrinos, Pope, Shen, & Schwebel, 2017). Furthermore, practice effects (i.e., main effect of time) were not found for driving simulator outcomes, suggesting that baseline to post-test learning was minimal, adding more support for the medium to large training effect sizes found for lane deviations and average driving speed.

Although these significant findings support the role of the frontal lobes and the response driven and goal-directed behavior of driving, namely the ventral frontal cortex, prefrontal cortex, and the premotor cortex, given the limited focality and widespread effects of the conventional tDCS technique used in the current study (Kessler et al., 2013; Minhas et al., 2010; Minhas et al., 2012; Woods et al., 2016), regional specificity of these individual frontal areas cannot be determined. Previous research has shown an association between the DLPFC and premotor cortex and driving behavior, suggesting the role of cognitive control and preparatory motor responses in responding to stimuli in the driving environment (Graydon et al., 2004; Spiers & Maguire, 2007). Less is known about the role of the ventral frontal cortex, particularly the rIFC, and its association with risk-taking behavior; specifically the role of the salience network, which aids in the filtering and orienting of attention to relevant stimuli (Menon, 2015). Furthermore, the salience network has been associated with mediating the switching between the central executive and the default mode network by detecting relevant salient events and initiating a sequence of signals, engaging the central executive and suppressing the default mode network (Goulden et al., 2014; Menon, 2015; Sridharan et al., 2008). Regarding driving, associations between the ventral frontal cortex and risky driving behavior have not previously been found (Spiers & Maguire, 2007), but these areas may play a role in detecting and switching attentional focus to key, safety-related stimulus, aiding in the overall regulation of safe or cautionary driving behavior. While these findings and the mechanisms behind them need further investigation, the associations between the frontal lobe areas, salience network, and default mode network may help to explain the effects seen with combination tDCS SOP-CRT.

There are three notable limitations of needed discussion that may have contributed to the findings. First, a full factorial design (i.e., a true control group, SOP-CRT only group, and tDCS only group) was lacking. While these methodological arms are needed for a full assessment on the effect of combination tDCS SOP-CRT on simulated driving performance, the study was a preliminary, pilot study which assessed feasibility of a CRT of this nature in a clinical population know to have deficits in SOP (Fazeli, Marceaux, Vance, Slater, & Long, 2011; Vance et al., 2012) and be at risk for decrements in driving performance (Marcotte et al., 1999; Marcotte et al., 2004; Vance et al., 2014). The second limitation, sample size also relates to the preliminary nature of the study. While the sample size was small, it was consistent with other tDCS studies and larger than both Beeli et al. (2008) (n = 24) and Sakai et al. (2014) (n = 13) which also focused on simulated driving outcomes. Furthermore, while recruitment efforts focused on a representative HIV sample in the Southeast United States, HIV samples are heterogeneous across the nation and globally. Currently, our sample of mostly African American males is reflective of PLWH in Alabama (Alabama Division of

STD Prevention and Control, 2014; Centers for Disease Control and Prevention (CDC), 2014). Future investigation is needed in larger sample sizes.

Lastly, one notable limitation that could have aided in lack of effects on driving outcomes was the usage of the monopolar montage with the anode placed over the F10 with the cathode on the contralateral left shoulder. This montage corresponds to stimulation of the ventral frontal cortex related to attentional shift from a focal point to an unexpected stimuli (Fox et al., 2006; Vossel et al., 2014), and would result in an overall broad range of stimulation of the frontal lobe with less focal effects from the return electrode, but possible dampening of the stimulation due to the distance from the stimulating electrode (Coffman, Clark, & Parasuraman, 2014). Furthermore, this electrode placement followed other training paradigms that targeted complex behavior, attention, and learning (Clark et al., 2012; Coffman, Trumbo, & Clark, 2012; Falcone, Coffman, Clark, & Parasuraman, 2012). The F10 with contralateral left shoulder montage differs from previous tDCS studies focusing on cognitive processing (Coffman et al., 2014) and driving (Beeli et al., 2008; Sakai et al., 2014) as many use a more focalized approach, stimulating the DLPFC (F3/F4), an area of the frontal cortex related to higher-order cognitive processing, such as executive function (Banich, 2009). Further studies should target F3/F4 in the context of combination tDCS SOP-CRT for comparative effects between widespread frontal lobe stimulation and a more targeted simulation of a specific frontal lobe area.

5. Conclusion

Employing a combination tDCS SOP-CRT intervention, active tDCS SOP-CRT over 10 hours was found to increase cautionary simulated driving behavior in older PLWH. While findings warrant further investigation using different methodological designs and larger sample sizes, they extend previous research focusing on tDCS and its applicability using complex real-world behaviors. Findings expose an avenue of intervention and rehabilitation regarding driving performance which may improve injury prevention efforts and improve quality of life for the aging population.

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- Effects of tDCS SOP-CRT on simulated driving outcomes were investigated.
- Large training effect on average driving speed found for active tDCS SOP-CRT.
- Marginal medium training effect on lane deviations found for active tDCS SOP-CRT.
- Combination tDCS SOP-CRT increases some indices of cautionary simulated driving.
- Potential avenue of intervention and rehabilitation for vulnerable road users.

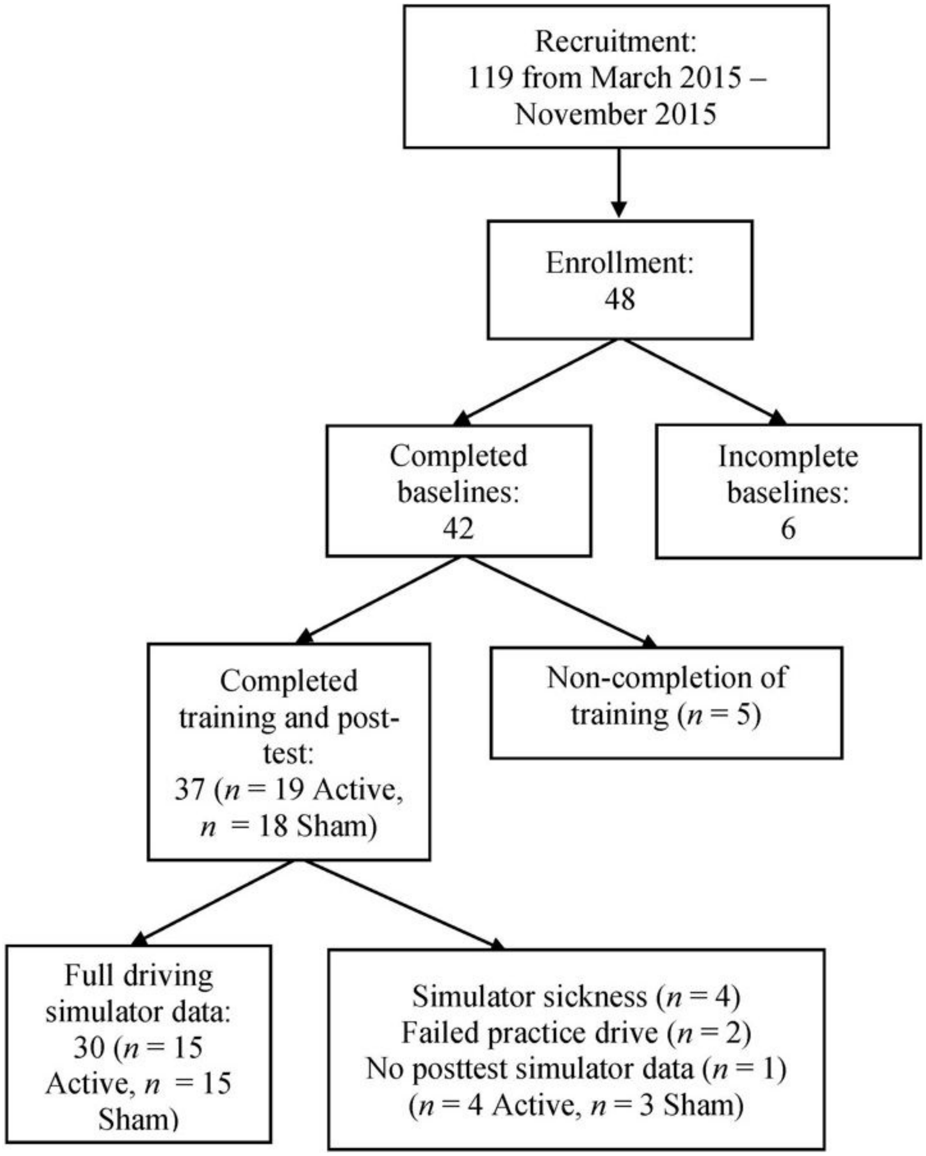

Fig. 1.
Study recruitment chart.

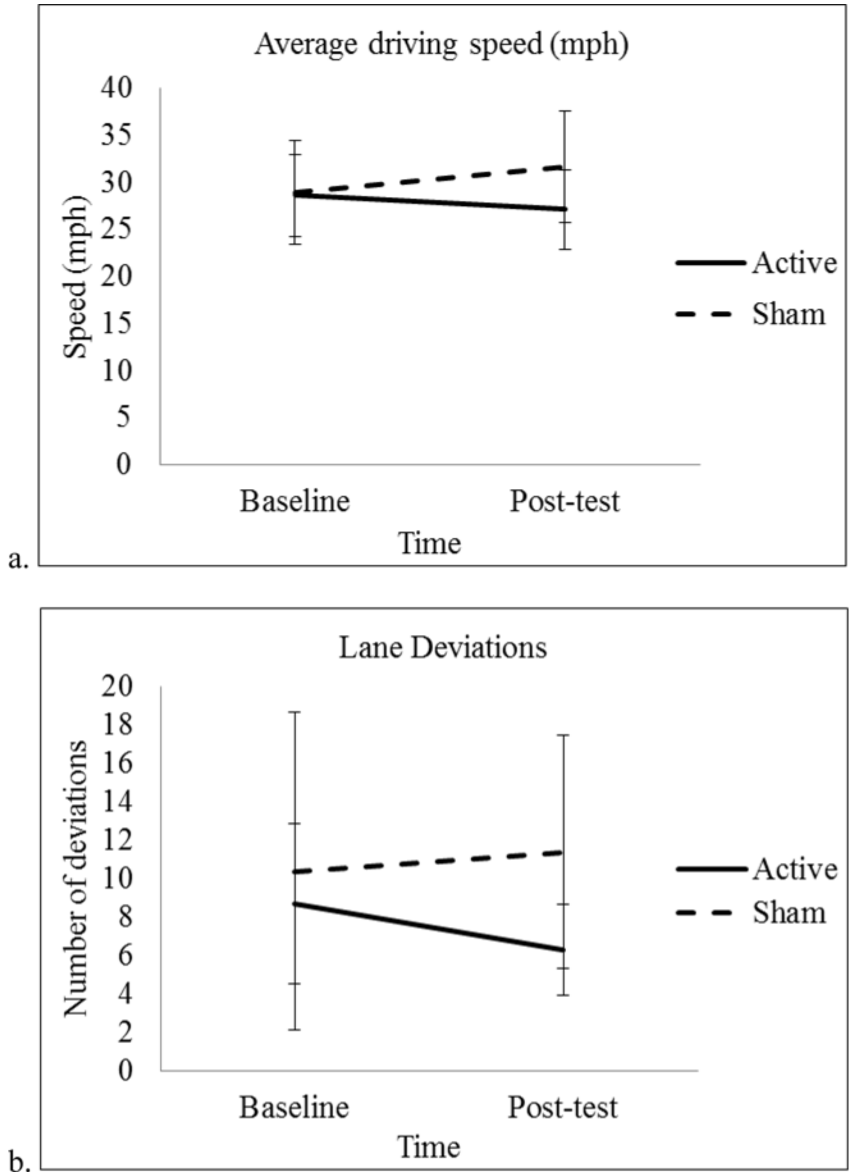

Fig. 2.
Interaction of time and training group on average driving speed (a) and lane deviations (b).

Table 1

Sample characteristics.

	Total Sample (n = 30)	**Active tDCS SOP-CRT (n = 15)**	**Sham tDCS SOP-CRT (n = 15)**		
Variable	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*t* (*df*)	*p*
Age	54.53 (3.33)	55.33 (3.33)	53.73 (3.24)	−1.33 (28)	0.193
Years of education	12.40 (1.85)	12.53 (1.88)	12.27 (1.87)	−0.39 (28)	0.700
Days driven per week	3.27 (3.17)	4.27 (3.17)	2.27 (2.94)	−0.79 (28)	0.084
Time since HIV diagnosis (years)	16.30 (7.63)	17.20 (7.23)	15.40 (8.15)	−0.64 (28)	0.528
Most recent prior CD4 lab	749.53 (431.97)	751.00 (334.98)	748.07 (523.74)	0.02 (28)	0.986
Time since most recent prior CD4 lab (days)	131.17 (112.54)	121.47 (91.32)	140.87 (133.02)	0.47 (28)	0.645
Nadir CD4 lab	174.93 (203.48)	172.33 (226.58)	177.53 (185.50)	−0.07 (28)	0.946
Total trained:					
Minutes	583.97 (48.04)	581.00 (61.68)	586.93 (30.92)	−0.33 (28)	0.742
Days	9.70 (0.99)	9.60 (1.30)	9.80 (0.56)	−0.55 (28)	0.588
Training duration (baseline to post-test in days)	22.07 (6.12)	21.07 (4.67)	23.07 (7.32)	−0.89 (28)	0.380
Time from post-test from last training session (days)	3.30 (3.30)	2.33 (1.59)	4.27 (4.25)	1.65 (28)	0.110
	%	%	%	χ^2	*p*
Gender (male)	63.3	66.7	60	0.14	0.705
Race (African American)	86.7	80.0	93.3	1.15	0.283
Valid and current	53.3	73.3	33.3	5.99	0.014*
driver's license (yes)[a]					
Viral load lab (% undetectable)	93.3	93.3	93.3	0.00	1.00

[a]*Notes*. Total $n = 29$ ($n = 14$ Active tDCS and SOP-CRT, $n = 15$ Sham tDCS and SOP-CRT).

SOP-CRT = Speed of processing cognitive remediation therapy.

Table 2

Simulated driving performance.

	Total Sample		**Active tDCS SOP-CRT**		**Sham tDCS SOP-CRT**	
	M (*SD*)		*M* (*SD*)		*M* (*SD*)	
Variable	Baseline	Post-test	Baseline	Post-test	Baseline	Post-test
Lane deviations	9.53 (6.50)	8.83 (5.23)	8.67 (4.17)	6.27 (2.37)	10.40 (8.27)	11.40 (6.07)
Violations	12.03 (7.43)	12.07 (6.14)	12.60 (8.47)	11.13 (5.89)	11.47 (6.47)	13.00 (6.45)
Collisions	2.20 (1.03)	1.83 (0.99)	2.13 (0.99)	1.80 (1.01)	2.27 (1.10)	1.87 (0.29)
Hazard RT	0.92 (0.38)	0.89 (0.40)	0.96 (0.46)	0.86 (0.31)	0.88 (0.29)	0.91 (0.47)
SDLP	0.82 (0.38)	0.93 (0.39)	0.79 (0.32)	0.88 (0.32)	0.84 (0.45)	0.98 (0.46)
Average driving speed (mph)	28.80 (1.90)	29.41 (5.57)	28.63 (5.50)	27.12 (5.92)	28.97 (4.40)	31.71 (4.24)
SD of speed (mph)	12.59 (1.66)	12.81 (2.40)	12.41 (1.82)	12.18 (2.44)	12.77 (1.51)	13.44 (2.27)

Notes. SOP-CRT = Speed of processing cognitive remediation therapy; SDLP = standard deviation of lane positioning; RT = reaction time; mph = miles per hour. Simulated driving performance metrics are operationally defined in section 2.3.2. STISIM Driving Simulato r.

Table 3

Repeated Measures ANOVA (RM-ANOVA) – Interactions with time.

	F	*df*	*p*	η^2	*d*
Lane Deviations					
Driver License Status	0.003	1	0.954	0.000	0.000
Training Group	2.671	1	0.114	0.093	0.640
Violations					
Driver License Status	0.496	1	0.488	0.019	0.278
Training Group	0.532	1	0.472	0.020	0.286
Collisions					
Driver License Status	2.230	1	0.147	0.079	0.586
Training Group	1.041	1	0.317	0.038	0.398
Hazard RT					
Driver License Status	1.408	1	0.246	0.051	0.464
Training Group	0.016	1	0.901	0.001	0.063
SDLP					
Driver License Status	5.004	1	0.034	0.161	0.876
Training Group	1.719	1	0.201	0.062	0.514
Average driving speed (mph)					
Driver License Status	0.217	1	0.646	0.008	0.180
Training Group	6.127	1	0.020	0.191	0.972
SD of speed (mph)					
Driver License Status	3.699	1	0.065	0.125	0.756
Training Group	0.060	1	0.809	0.002	0.090
Error		26			

Notes. SDLP = standard deviation of lane positioning; RT = reaction time; mph = miles per hour. Simulated driving performance metrics are operationally defined in section 2.3.2. STISIM Driving Simulator.