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Original Research Article

Effects of a Motor Cortex Neuromodulation Approach on Neuromotor and Neurocognitive Performance in Latinx People with HIV

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Abstract

Background: Human Immunodeficiency Virus (HIV) infection has been known to impact both motor and cognitive systems and cause motor and cognitive alterations (MCAs). Transcranial direct current stimulation (tDCS), mainly when applied to the prefrontal cortex, has shown promising results in improving gait, balance, and executive functions in individuals with HIV. Previous studies suggest that integrating a task designed to stimulate higher cognitive centers in combination with tDCS could potentially enhance these effects. ***Purpose***: The objective of this study was to investigate whether the combination of tDCS with a tracking task, when applied to the prefrontal cortex, effectively enhances reaction time and HIV dementia scale (HDS) scores (motor-cognitive) components in individuals living with HIV. ***Methods***: The study involved nine female and one male participants living with HIV, with an average age of 58.9 Â± 4.3 years. To assess the impact of tDCS on RT and motor cognition, each participant was evaluated both before and after the administration of tDCS with the HDS. Participants' primary goal for the reaction time components was to respond quickly and accurately to color changes by tapping the pod that lit up green. This task was performed while applying tDCS to the prefrontal cortex, allowing researchers to focus simultaneously on cognitive reaction speeds and the physical effects of neuromodulation. ***Results:*** Upon analysis, significant differences were noted between pre and post-tDCS of the HDS scores. The data further revealed substantial improvements in reaction time, hits, and strikes after the tDCS application. ***Conclusion:*** The results of this study demonstrated that tDCS can potentially improve neurocognitive and motor function in individuals with HIV. However, the study recommends that tDCS treatments be applied over a more extended period than in this study.

Keywords: Motor-cognitive Alterations, Supraorbital neuromodulation, Gait Deviations, HIV- Complications, Motor control Deficits, HIV dementia.

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INTRODUCTION

Human Immunodeficiency Virus (HIV) infection continues to pose a significant global health challenge, affecting millions worldwide, as reported by UNAIDS in 2021. Despite advances in antiretroviral therapy (ART) transforming HIV into a chronic, manageable condition, it still profoundly impacts neurological functions. This above issue leads to a range of cognitive impairments, termed HIV-associated neurocognitive disorders (HAND), as highlighted by Heaton *et al.*, in 2010. HAND impacts several components that could impair activities of daily living such as memory and psychomotor speed among others as stated by Antinori *et al*., 2007. Even with effective ART treatment approximately half of PLHIV experience these problems, which is a concern in the aging HIV-infected population (Vance *et al*., 2011; Rosario and Orozco *et al*., 2021). A major component altered in those living with HIV is reaction time (RT), which involves motor speed and coordination (Ogunrin, O., & Odiase, F. 2006). RT estimates the interval between a stimulus and the associated responses, which is related to the abovementioned motor speed and coordination components (Gonzalez-Casanova, I., & López-López, M., 2019). RT is an important measure in various settings such as healthcare and for research purposes based on the implications.

RT can involve a single or multiple stimulus and responses (Reigal *et al*., 2019) and provide a measurement of cognitive processing speed, therefore is vital for daily decision-making and motor coordination (Deary *et al*., 2001). Research shows that PLHIV has longer RTs, particularly with double cues. Various factors are linked to altering RT such as neurocognitive deficiencies and depression among others which are more prevalent as those that survive HIV grow older, making other health issues arise and extensively more impactful (Wang *et al*., 2017). Depression, which is common among HIV-positive individuals (Hyder & Rosario, 2021), can also affect concentration and focus, potentially impacting RTs (Goldschmidt R & Chu C, 2021). In those living with HIV neurocognitive problems usually come accompanied by motor deficiencies, related to gait, coordination, muscle control, and neuromuscular activation impairments (Rosario MG, 2020 & 2022; a-b,d; Rosario *et al*., 2020 a-c; 2021b; 2022c-d; 2023). The reason neuromotor and neurocognitive issues are difficult to treat is because they are complex and multifactorial, involving not only the peripheral nervous systems (Rosario *et al*., 2021a) but also the central nervous systems (Robinson-Papp *et al*., 2008; Letendre, 2011; Cysique *et al*., 2004; Vance *et al*., 2011).

Transcranial direct stimulation (tDCS) has emerged as a promising non-invasive technique in managing neurocognitive and neuromotor deficiencies. Studies support this approach, indicating its potential in various neurological treatments (Rosario *et al*., 2022b & 2024; Bikson *et al*., 2016). Although its implication and benefits in HAND is not yet well explored, a study by Rosario and colleagues (2022b; 2024), revealed tDCS significantly improved gait speed and postural sway after five treatment sessions. These results underscore the prospect of tDCS as a therapeutic tool for improving motor function in individuals with HIV, however, highlighting the importance of further research to understand the mechanisms behind these improvements and optimize treatment protocols for maximal benefit.

tDCS was proven to be effective in Alzeimer improving cognitive components resembled to those in the sham group. This study suggested that tDCS might influence cortical plasticity, making it a valuable tool for neurocognitive rehabilitation (Rezakkani *et al*., 2024). In a study examining tDCS's impact on working memory, researchers found that the electrode montage used during treatment could affect its efficacy. High-definition tDCS could offer more precise modulation of brain functions than traditional bipolar tDCS. This insight could guide future applications and inform the optimal setup for cognitive improvement (Ke Y *et al*., 2019).

Based on the above and Rosario *et al*.,'s (2022b) research, this study asserts that tDCS with targeted neurocognitive activities will significantly improve RTs after prefrontal neuromodulation. This hypothesis is grounded in the emerging understanding that combining neuromodulatory techniques and cognitive exercises can synergistically enhance neural efficiency, particularly in the prefrontal cortex, which is crucial for processing speed and cognitive function. The rationale behind this approach is that while tDCS alone can enhance neurocognitive (HDS) and neuromotor (gait), its effects can be substantially augmented when coupled with cognitive tasks that specifically activate the stimulated brain regions. This hybrid strategy could lead to more pronounced and sustained improvements in cognitive functions, such as RT, a critical measure of cognitive health and efficiency.

METHODS

This study was conducted at the HIV Latino/Hispanic Community Fitness Center in La Perla Precio, San Juan, Puerto Rico. Participation eligibility required individuals to consent to access their medical records, disclose their HIV status, and provide their CD4+ cell counts. The Institutional Review Board approved this research under Approval No. FY2020-32. All participants had to provide written informed consent before being included in the study.

Before commencing the experimental procedures, researchers obtained comprehensive demographic data from each participant, including age, sex, duration of HIV diagnosis, results from the timed 5x sit-to-stand test to assess lower limb strength, and the Fukuda test to evaluate for vestibular disorders. The participants' characteristics and the study's design are systematically detailed in Table 1.

The cohort consisted of 10 rigorously screened individuals with an average age of 58.9 Â± 4.3 years, all diagnosed with HIV. Each participant was interviewed, and their medical records were evaluated against specific inclusion and exclusion criteria. The inclusion criteria included:

Being between 25 and 80.
Having a confirmed HIV diagnosis.
Having a CD4 count above 200 cells/ÂµL.
The ability to perform a 5-time sit-to-stand test.
Being able to walk independently without an assistive device.
The exclusion criteria included:
Untreated severe visual impairments.
Significant balance disorders.
A CD4 count below 200 cells/ÂµL.
Recent use of sedative medications within the last 24 hours before the intervention.
A history of falls in the previous six months.
Being pregnant or potentially pregnant.
Balance assessments using the Romberg Balance Test required participants to stand with closed eyes for 30 seconds.

tDCS Protocol: Following the guidelines established by Rosario *et al*., (2022), the tDCS protocol involved two battery-operated electrical stimulators attached to the participants' foreheads using headbands and 35-cm^2 synthetic sponges moistened with saline to enhance conductivity. The cathode (negative charge) was placed above the left frontal bone's supraorbital margin, and the anode (positive charge) was located over the right frontal bone's supraorbital margin. Each session lasted 20 minutes and was administered three times within the same week, with one rest day in between sessions. The electrode current started at 0.5mA and was manually increased to 2.0mA. Participant safety was prioritized, with individuals encouraged to report discomfort during sessions. The tDCS device current was reduced to 0 mA at the end of each session. Finally, the above protocol was selected based on the results on other populations related to stroke, Alzheimer's disease, and HIV patients (Costa *et al*., 2015; Boggio PS *et al*., 2009; Rosario *et al*., 2022b & 2024).

Visual Cognitive Technology (RT Assessment): The RT assessment utilized five strategically positioned Blaze Pods approximately 6 inches apart (https://www.blazepod.com/), each capable of changing colors. The primary objective for participants was to respond or react to color shifts by tapping the pod that displayed a red light while the other 5 pods turned on with different colors (blue, green, yellow) for 1.5 minutes. This specific activity was designed to measure the mental processing speed and motor response accuracy of participants, providing valuable insights into the cognitive impacts of HIV and the potential therapeutic effects of tDCS.

Data Analysis

RT Components: Scores for RT were collected during each session and systematically organized in an Excel spreadsheet for thorough analysis. A repeated measure Analysis of Variance (ANOVA) was used to explore relationships between data points, including RT (measured in milliseconds), hits (number of taps), misses, and strikes (forceful near-misses). A p-value of 0.05 or less was used as a threshold for statistical significance to evaluate any cognitive improvements resulting from tDCS treatments.

RESULTS

Table 1 outlines the demographic characteristics of the study group, consisting of 9 females and one male with an average age of 58.9 Â± 4.3 years. The average age for individuals diagnosed with HIV was 27 years, with a mean CD4 count of 792.3 Â± 192.01.

Table 2 compares the HDS and RT data. The results of the Multivariate Analysis of Variance (MANOVA) in Table 2 show significant differences in HDS between the beginning and end of tDCS treatment (day 1 vs. day 5), with a p-value less than 0.01 indicating statistical significance. A repeated measures Analysis of Variance (ANOVA) was conducted to analyze RT, hits, misses, and strikes, comparing day 1 with days 2-5 of treatment. Results indicated a significant difference in RT between day 1 and day 5 ($p < 0.01$), an increase in hits from day 1 to days 4-5 ($p < 0.05$), and fewer strikes from day 1 to day 5 ($p < 0.05$). The data for misses was consistent across the treatment period.

Table 1: Demographic data of all participants

Characteristics	
Age (years)	M = 58.9 ± 4.3
Gender	9 females 1 male
Year of Dx (years)	M= 27 +/-6.2
Cd4	M= 792.3 ± 192.01
Weight	199.4 ± 77.6
Height	5.1± 0.3 (feet) / 4.3± 2.5

Table 2: Comparison of neurocognitive and neuromotor profile after tDCS. Results of repeated measures ANOVA performed comparing tasks. Significance level set at p≤0.05

Variables	D1 Treatment	D5	P-Value
HDS	7.8 ±2.2	10.9± 1.2	0.01
Reaction Time Data			
	D1	Treatment days	P-Value
Hits	34.9 ± 7.8	D2- 38.1± 7.2 D3- 39.5± 11.9 D4- 40.3± 9.7 D5- 42.6± 8.6	0.18 0.11 0.05* 0.05*
Missed	9.2 ± 5.1	D2- 7.7±4.2 D3- 8.1± 6.4 D4- 7.4±5.2 D5- 6.7± 4.6	0.24 0.49 0.09 0.19
Strikes	1.6 ± 1.4	D2-0.81± 1.5 D3- 0.90± 1.2 D4- 0.82± 0.98 D5 0.61± 9.66	0.18 0.26 0.18 0.05
Reaction Time (milliseconds)	1075.9 ± 52.8	D2- 1054.3± 69.6 D3- 1003.4±78.7 D4- 1013.5± 73.8 D5- 973.57± 89.5	0.66 0.11 0.06 0.01
ms=milliseconds, D=day, HDS=HIV dementia scale			

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DISCUSSION

The current study aims to propose a treatment to aid or reduce some of the MCAs in PLHIV. Based on recent findings related to the benefits of tDCS by Rosario *et al*., (2022) on neuro components mentioned before, the current inquiry hypothesized that tDCS in conjunction with a neurocognitive activity will lead to enhanced RTs following prefrontal neuromodulation. The results of the current study showed that integrating a dual focus on cognitive reaction in conjunction with neuromodulation improves MCAs such as RT. Therefore, we accepted our previous assumption.

The necessity for novel methods, such as tDCS, to improve motor-cognitive abilities in individuals with HIV, is derived from the virus's deleterious effects on both the immune and nervous systems. These effects lead to neurological disorders and alteration to brain structures essential for motor and cognitive functions, significantly impairing daily living activities (Sullivan E *et al*., 2011; Heinze B *et al*., 2013). As pointed out before, ART has been identified as a treatment to curb the progression of MCAs. ART has not only extended life and survival rates for over a decade in people living with HIV (Woods SP *et al*., 2009), but also increased the probability of motor-cognitive impairments associated with the virus (Watkins CC *et al*., 2015). Therefore, mild neurological modifications remain prevalent and negatively impact the quality of life (Havlik RJ *et al*., 2011; Cross S *et al*., 2013). These MCAs are characterized by affecting motor speed, information processing, executive functions, attention, learning, memory, and information retrieval, and are notably pronounced in HIV (Woods SP *et al*., 2009; Dawes *et al*., 2008).

The initial finding of this study highlighted an improvement of RT, which improved consistently with each tDCS session, demonstrating the efficacy of prefrontal neuromodulation in this cohort following a five-day tDCS at 2mA for 20 minutes. As documented in the literature, this specific timing and electrode placement used in this study has been previously establish as effective in neurocognitive interventions across various conditions, including stroke (Lindenberg R *et al*., 2010; Costa V *et al*., 2015; Nelson JT *et al*., 2014; Sandrani M *et al*., 2016; Vines BW *et al*., 2006), Parkinson's disease (Boggio PS *et al*., 2006), Alzheimer's disease (Boggio PS *et al*., 2009), and HIV-affected individuals (Rosario et al., 2022, 2024).

Research related to tDCS supports its application in individuals with mild cognitive impairment, Parkinson's disease, and those recovering from stroke. tDCS has significantly improved cognitive functions, including processing speed, task planning, selective attention, and memory, among older adults experiencing mild motor-cognitive alterations (Gonzalez *et al*., 2017). Additionally, the anodal tDCS approach, when combined with physical training, shown to improve motor performance and RT in healthy individuals and those with neurological disorders (Wang *et al*., 2021).

Furthermore, research into combining exercise with tDCS to improve cognitive function in individuals with mild cognitive impairment and Alzheimer's disease showed encouraging results. This combined approach indicated that tDCS and exercise might improve cognitive outcomes through neurogenesis and angiogenesis, suggesting new avenues for enhancing treatment effects (Lui *et al*., 2021). Nevertheless, regardless of the results of the current study, researchers focus on the use of tDCS in the HIV population is somewhat limited, with most studies focusing on alleviating depressive symptoms. These earlier studies highlighted the need for more extensive research to understand the underlying mechanisms of tDCS within PLHIV (Fazeli *et al*., 2017; Ownby & Acevedo, 2016; Knotkova *et al*., 2012).

CONCLUSION

The current study aimed to examine the benefits of combining prefrontal cortex neuromodulators with RT tasks, focusing on the simultaneous assessment of cognitive RTs and the physiological effects of neuromodulation. This investigation ushered in using tDCS on the prefrontal cortex and RT cognitive task, which allowed us to explore both cognitive and motor outcomes in individuals living with HIV. This approach may prove valuable in clinical settings by aiding treatment decisions and enabling early intervention for PLHIV. Monitoring RT regularly could help identify those at risk of cognitive decline and guide appropriate modifications to ART regimens or other therapies to mitigate neurocognitive impairment. Integrating RT assessments with traditional neurocognitive evaluations, such as the HDS, enhances the sensitivity of neurocognitive screening for PLHIV.

Finally, these neuromodulation approaches could offer insights into the neurobiological mechanisms underpinning HIV-related cognitive impairments, such as neuronal and white matter abnormalities. All the above underlines the need for comprehensive care strategies and ongoing research to improve treatment outcomes for those with MCAs. Future studies should look into adding physical activity such as walking with the use of tdcs to better comprehend the impact of a motor and cognitive task pair with neuromodulation.

Declaration:
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Conflicts of interest/Competing interests: Authors report no conflict or competing interest.

Ethics Approval: IRB approval TWU protocol #FY2020-32

Consent to Participate: The participant gave signed consent for this study

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