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Prefrontal Cortex Neuromodulation Improves Standing Balance in Latinx Hispanic People Living with HIV

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Abstract

Human Immunodeficiency Virus (HIV) attacks the immune system and is typically managed with antiretroviral medication (ART). This virus has been known to cause both neuromotor issues, such as difficulties with gait and balance, as well as neurocognitive problems, including memory issues, in those who are affected by the disease. The evidence indicates a correlation between an increase in life expectancy and the development of neurological motor problems, resulting in a decline in the overall quality of life. Apart from ART, there are limited treatment options available to mitigate motor-cognitive decline in HIV patients.

Purpose: To investigate the effect of transcranial direct current stimulation tDCS on postural instability in Latinx living with HIV.

The study enrolled 11 participants, aged 59.9 +/- 5.2 years, who had been diagnosed with HIV and had a CD4 count of 814.4 +/- 235.8. These participants had been diagnosed with HIV for an average of 27.8 +/- 6 years, and were recruited from La Perla de Gran Precio, an HIV non-profit fitness clinic in Puerto Rico. We gathered standing postural data utilizing gyroscopes and accelerometers before and after transcranial direct current stimulation tDCS. The prefrontal tDCS protocol consisted of a five-day treatment, with each session lasting 20 minutes at a current intensity of 1.5 mA.

The results encompassed tasks related to balance, such as sway (area of movement), velocity, distance, and direction. We analyzed the balance data points both before and after the tDCS intervention, and found a tendency towards reduced sway in terms of direction, distance, and velocity.

Conclusion: The utilization tDCS demonstrated encouraging outcomes and could potentially serve as a feasible and secure treatment alternative for those diagnosed with HIV and suffering from postural instability. The forthcoming inquiry should consider the potential benefits of incorporating tDCS in conjunction with various forms of training that involve cognitive or mental processes.

Introduction

As stated by the World Health Organization (WHO), the human immunodeficiency virus HIV infection is a complex and chronic disease that targets the immune system, causing severe damage and weakening the body's ability to fight off infections and diseases. This virus attacks the immune system by destroying CD4 cells, which trigger the body to fight infection. There is currently no cure for acquired immunodeficiency syndrome (AIDS), a potentially life-threatening condition caused by untreated HIV. A positive development is that individuals infected with HIV can effectively manage their condition through appropriate medical treatment, enabling them to lead healthy lives [1].

Encouragingly, studies have demonstrated that medications for antiretroviral treatment ART in HIV has markedly enhanced prognosis and quality of life by suppressing HIV replication [2]. According to a study by Rojas-Celis et al. [3], the use of ART has slowed down the progression of the disease. Despite these facts, HIV infected people continue to face functional impairments, as reported by Rosario et al. [4-6]. HIV remains a serious and pressing health concern, despite the numerous advantages of ART. Furthermore, as stated by Rosario et al., [7], ART had been linked to potential adverse outcomes including abnormal heart rate, muscle pain, weakness, and the accumulation of lactic acid in the body. Although ART has shown the capacity to mitigate the impact of the disease on the motor-cognitive system, HIV remains detrimental to normal cognitive function, gait, and balance stability, thereby increasing the susceptibility of falls and premature mortality in affected individuals [8].

The occurrence of motor-cognitive impairments can be attributed to the replication of HIV within the brain, resulting in inflammation in the frontal lobe, particularly in the motor-cognitive cortex [9, 10]. The presence of HIV has a significant impact on gray matter structures and subcortical regions, resulting in disruptions to motor, cognitive, and behavioral functioning. A study by Rosario et al. [11] found that motor impairment remains present in patients with HIV, and tends to worsen with advancing age.

To date, no treatment has fully addressed the neurocognitive and neuromotor development associated with this disease. However, recent studies have shown that transcranial Direct Current Stimulation tDCS may be a potential treatment option for PLHIV [12]. This is a technique that can modulate neural firing by altering the polarity of the axon membrane potentials, which can potentially have significant effects on brain function and behavior. By decreasing the membrane polarity, the excitation response of neighboring axons upon stimulation or depolarization occurs more quickly. Theoretically, an increase in neural firing rates can increase the excitability of spinal neural circuits, thereby contributing to movement and neuroplasticity [13]. Although there has been a growing amount of research on the effects of tDCS over the last 50 years, there is a need for further research on tDCS in PLHIV.

The purpose of this study was to analyze motor adaptations in PLHIV during single-limb stance tasks after tDCS intervention. Studies have shown that single-limb balancing training alone improves balance control [14]. However, the role of tDCS in HIV-related neuromotor deficits, such as postural control and sensory systems connected to balance, remains poorly understood. Therefore, this study attempts to answer the question: Does prefrontal cortex tDCS treatment impact standing balance in PLHIV? Understanding the influence of tDCS on motor control and the effects of HIV on balance in PLHIV could help determine an optimal treatment plan and, consequently, improve quality of life.

Method

Study protocol for data collection was conducted at a HIV Latino/ Hispanic Non-Profit Fitness Center, called La Perla de Gran Precio, located within the city of San Juan, Puerto Rico. In order to access the CD4+ cell counts, HIV status, and medical records, it is necessary for individuals to provide informed consent as a form of participation.

Eleven PLHIV, with an average age of 59.9+/- 5.2 years, were recruited for the present study. This study was approved by Texas Woman's University IRB (protocol #FY2022-210). Every individual involved in the study carefully read and if agree to be part of the study, sign the informed consent form. Next, was performed a thorough evaluation based on specific inclusion and exclusion criteria, which was conducted through both an in-depth interview and a comprehensive review of their personal medical records. In order to be eligible for participation in this study, individuals had to meet a set of specific criteria, including: 1) confirmed diagnosis of HIV, 2) CD4 levels above 200 cells/µL, 3) age range between 25 and 80 years old, 4) ability to walk without assistance, and 5) Successful completion of a 5-time sit-to-stand test once. The criteria for exclusion 1) a history of falls within the past six months, indicating a potential risk for further falls during the study, 2) recent use of medications with drowsy side effects, which could interfere with the participant's ability to fully engage in the study tasks, and 3) women who were pregnant or possibly pregnant. Upon thorough examination of the screening process, a total of 11 adults (3 males and 8 females), were eligible to participate in the study.

A lumbar accelerometer was used to assess their balance. The collected balance data was gathered by the MobilityLabTM, which is owned and operated by APDM Inc. Throughout the experiment, measurements of the anteroposterior (AP) and mediolateral (ML) sway directions, distances, and velocities were recorded and gathered for analysis. As a precautionary measure, a researcher positioned as a spotter behind the participant to prevent any potential falls during the balance testing. In the event that participants experienced a loss of balance, they utilized their contralateral limb to regain balance and proceeded with the trial. The quantity of foot touchdowns on the opposite limb was documented during each trial. This tally did not encompass additional actions aimed at restoring equilibrium, such as gesturing limbs, tilting to one side, or hopping on the examined lower extremity.

The balance protocol used in this study was based on a previously published protocol by Rosario et al. [15], providing a solid foundation for our research. The initial phase of the protocol involved an evaluation that included a single task on a solid surface as a reference point, followed by four tasks conducted on a thick foam pad placed on a hard surface, with an emphasis on individual task performance. The conditions for each task were as follows:1-2) eyes open (EO) focusing on a fixed point on the wall while standing on a 1) hard floor surface and 2) a thick foam pad to alter somatosensory function; 3) eyes closed (EC) while standing on a thick foam pad (with the head fixed at approximately 90 °) to alter somatosensory function and remove visual input; 4) EO focusing on a fixed point on the wall, while actively moving the head upward and downward at a 45-degree angle in each direction to alter vestibular inputs (head movement rhythm was maintained with a metronome at 60 bpm); and 5) EC (with the head fixed at approximately 90 °) with active upward and downward head movements (with head movement rhythm as described in task 4) to cancel visual input and modify vestibular inputs.

The tDCS protocol utilized two battery-operated electrical stimulators, which were connected to the patient's forehead using a headband and a pair of synthetic sponges with a saline solution for conductivity, measuring 35 cm^2 in size. The anode, or positive electrode, was positioned above the supraorbital margin of the right frontal bone, while the cathode, or negative electrode, was placed over the corresponding area on the left. The tDCS treatment comprised of five intervention sessions, of 20 minutes each, occurring three times a week over the course of two weeks. Due to the direct application of electrical currents to the skin, the current was manually raised from 0.5 mA to 2.0 mA as a precautionary measure. All participants were instructed to report any discomfort or concerns at any time during the study for further evaluation and precautionary measures as part of the safety protocol. The electrode placement and timing utilized in this study were determined based on tDCS which have been demonstrated to be effective in previous neurocognitive studies involving stroke patients [16], Alzheimer's disease patients [17], and individuals with HIV [18].

Statistical Analysis:

The data collected for balance analysis encompassed a wide range of measurements, including sway, anterior-posterior and medial-lateral jerk, velocity, and distance, for all of the balance tasks performed. The data pertaining to balance were inputted into the Statistical Package for the Social Sciences (SPSS) version 28 system in order to conduct a Multivariate Analysis of Variance (MANOVA) comparing the pre and post-tDCS treatment results. Descriptive statistics and pairwise comparisons were collected for the sway, AP, and ML jerk, as well as velocity and distance, during all five balance tasks. As a result of the thorough analysis conducted on the MANOVA, this study deemed a P-value of 0.05 or lower for the results to be significant.

Results

11 participants, aged 59.9 +/- 5.2 years

In Table 1, the demographic characteristics of study participants are presented. Within the sample group, there were 11 participants with an average age of 59.9 years old, with a standard deviation of ±5.2. Out of the eleven individuals present, two were males, while the remaining nine were females. The mean age at diagnosis was 26 years. The average CD4 count was 814.4 +/- 235.8 cells/mm^3.

Table 2 shows, no significant differences in the observed amount of sway. Nonetheless, there was a decrease in both the anterior-posterior and medial-lateral directions following the tDCS treatment.

In Table 3, a comparison of the jerk values is presented for both the anterior-posterior (AP) and medial-lateral (ML) directions. There were no notable discrepancies between the AP and ML directions. Despite this, upon conducting tDCS treatment, we were able to observe multiple emerging trends in both the AP and ML directions. The results showed a notably greater level of improvement in the AP direction compared to the ML direction.

Characteristics	
Age (years)	M = 59.9 ± 5.2
Gender	Male= 3 Female = 8
Year of Dx (years)	M= 27.8 +/-6.
Cd4	M= 814.4 +/- 235.8
Resting heart rate (RHR)	79 ± 15 beats per minute (bpm)
Resting oxygen saturation (SaO²)	96.45 ± 1.44%
Body mass index (BMI)	29.03 ± 8.10 kg/m².

Table 1: Demographic data of all participants.

Sway	Tasks	Pre tDCS Means and SD	tDCS Means and SD	P-Value
	DL: SLFirm: SLFirm ECHUD: SLFoam EOHUD: SLFoam EC:	0.26±0.11 1.44±0.87 1.76±0.41 2.47±1.30 2.26±1.02	0.32±0.24 1.12±0.67 2.15±0.86 1.93±0.88 2.11±0.69	0.09 0.67 0.19 0.31 0.22
^DL= ^SL= ^EO= ^EC= ^HUD= ^P=P-Value ^S.D.=Standard Deviation ^P-Value>.01 is not significant *P-Value≤.01 is significant S.D.=Standard Deviation				

Table 2: Comparison of sway between balance tests. Results of repeated measure ANOVA performed comparing tasks. Significance level set at p≤0.01

Jerk	Tasks	Pre tDCS Means and SD	tDCS Means and SD	P-Value
AP	DL: SLFirm: SLFirm ECHUD: SLFoam EOHUD: SLFoam EC:	2.25±2.19 308.33±400.86 472.00±338.34 1577.23±3623.16 589.31±703.83	10.26±25.21 301.41±429.91 1109.46±1042.30 764.15±744.41 811.00±948.04	0.44 0.69 0.47 0.91 0.10
ML	DL: SLFirm: SLFirm ECHUD: SLFoam EOHUD: SLFoam EC:	0.58±0.08 0.68±0.05 0.67±0.06 0.65±0.07 0.67±0.06	0.63±0.09 0.68±0.08 0.63±0.09 0.64±0.07 0.67±0.06	0.19 0.86 0.15 0.82 0.29
^DL= Double Limb ^SL= Single Limb ^EO= Eyes Open ^EC= Eyes Closed ^HUD= ^P=P-Value ^S.D.=Standard Deviation ^P-Value>.01 is not significant *P-Value≤.01 is significant S.D.=Standard Deviation				

Table 3: Comparison of Jerk AP and ML between balance tests. Results of repeated measure ANOVA performed comparing tasks. Significance level set at p≤0.01

In Table 4, velocities in both the AP and ML directions are presented. No significant differences were observed between the AP and ML directions. Nevertheless, there was a reduction in both directions after the tDCS treatment, with the most remarkable improvement in the AP direction. Table 5 presents a comparison of distances in the AP and ML directions. No significant differences were observed. However, after receiving tDCS treatment, study participants reduced both AP and ML directions in their movements. The observed improvement was more pronounced in the (ML) direction compared to the posterior (AP) direction.

Vel	Tasks	Pre tDCS Means and SD	tDCS Means and SD	P-Value
AP	DL: SLFirm: SLFirm ECHUD: SLFoam EOHUD: SLFoam EC:	0.13±0.08 0.74±0.56 0.81±0.48 1.17±0.72 1.39±0.90	0.18±0.16 0.53±0.28 0.98±0.62 1.05±0.66 1.07±0.52	0.16 0.19 0.25 0.29 0.36
ML	DL: SLFirm: SLFirm ECHUD: SLFoam EOHUD: SLFoam EC:	2.44±2.62 177.53±613.00 254.71±146.05 1521.57±3936.49 297.00±254.15	10.64±28.22 272.07±613.00 859.15±1137.60 586.95±771.34 500.40±730.75	0.76 0.39 0.99 0.54 0.53
^DL= ^SL= ^EO= ^EC= ^HUD= ^P=P-Value ^S.D.=Standard Deviation ^P-Value>.01 is not significant *P-Value≤.01 is significant S.D.=Standard Deviation				

Table 4: Comparison of Velocity AP and ML between balance tests. Results of repeated measure ANOVA performed comparing tasks. Significance level set at p≤0.01

Discussion

The research aimed to explore and provide insight into the impact of prefrontal cortex tDCS treatment on the standing balance PLHIV undergoing various balance tasks.

The act of standing on one leg, also known as single-limb stance (SLS), is a crucial aspect of motor and cognitive abilities for maintaining balance and gait. This aspect is particularly affected PLHIV as stated by Rosario et al. [4,19]. The static postural task of SLS is vital for daily living activities, and has been shown to be associated with improved balance control [20]. The task of SLS as it requires the integration of three sensory systems (vestibular, visual, and somatosensory) to maintain effective motor activation with a reduced base of support, as stated by Labanca et al. [21]. The combination and functionality of all these sensory systems play a crucial role in achieving and maintaining successful balance control. Research has indicated that the aforementioned components (vestibular and somatosensory)are modified for PLHIV, according to Rosario et al. [4-7,12,15,22].

Our results show that following tDCS, trend to decrease in sway was observed in both the (AP) and (ML) directions while maintaining a single-leg stance. Additionally, the results indicated a decrease in both distance and velocity when performing multiple complex balance tasks in both forward and backward directions. The tDCS led to a discernible enhancement in the equilibrium of the study participants. One potential explanation is that the intervention had a significant impact on the prefrontal cortex, ultimately enhancing standing motor control.

Rosario et al. (2020), it has been documented that PLHIV may experience neurological deficits that specifically impact their static postural control system. Additionally, PLHIV frequently demonstrate a reduced functional support system and diminished stability boundaries, which can significantly affect their capacity to carry out daily activities and sustain a sense of equilibrium. Rosario et al. [23] also reported that PLHIV experience postural instability as a result of an altered vestibular or neuromuscular system. Ryan et al. [24] revealed differences in outsize center of pressure sway, as well as the lower scores on the Berg Balance Scale and Dynamic Gait Index, in PLHIV compared to those without HIV in their study Furthermore, in a comprehensive analysis, the authors Berner et al. [25] conducted an in-depth examination of previous research that consistently demonstrated gait and balance impairments in PLHIV. The authors indicate that PLHIV exhibit heightened center-of-pressure excursions and longer latencies in their long-loop postural reflexes, particularly when presented with challenging conditions. In summary, PLHIV demonstrate postural instability as a significant complication that impacts their quality of life.

tDCS to the prefrontal cortex enhances balance and functional mobility for individuals with Parkinson's disease, particularly when compared to sham tDCS, as reported by Lattari et al. [26]. A systematic review also reported that tDCS of the dorsolateral prefrontal cortex and cerebellum improves dynamic balance and dual-task performance in older adults [27]. As previously mentioned, it has been noted that patients who suffer from both Parkinson's disease and stroke often have difficulties with their balance and gait. Lattari et al. [26] suggested that placing a tDCS on the left dorsolateral prefrontal cortex improves balance and functional mobility compared with sham treatment [26]. A study conducted by Dong et al. [28] revealed that tDCS enhanced walking independence, gait, and ambulation compared to a sham treatment.

In their study, Marotta et al. [29] examined the effects of tDCS on patients with multiple sclerosis, a disease that displays changes in cortical excitability, a characteristic also seen in PLHIV. The authors suggested that tDCS highly effective in improving gait and balance in individuals diagnosed with multiple sclerosis. This was demonstrated through significant improvements in the six 6-meter walk test after a two-week intervention period consisting of 20-minute tDCS sessions, conducted five days a week. The primary distinction between the cited studies and the present study lies in the activity component, as the placement of the tDCS electrodes was comparable. In our research, the participants remained seated during the entire tDCS treatment, compared to the dynamic activities simultaneously conducted alongside the intervention in the preceding studies. In conclusion, the application of tDCS to the prefrontal cortex has shown promising results for standing balance PLHIV.

Four muscle synergies use a single-limb stance: two ankle-dominant (tibialis anterior and soleus muscles) (peroneus longus and brevis), one knee-dominant, and one back/hip-dominant [30]. These muscle synergies make proper neuromuscular coordination and activation essential for balance [31]. According to Rosario et al. [4-7,12,15,22], research has indicated that the aforementioned components are modified for PLHIV. Therefore, it is recommended that future research examines the effects of tDCS on gait in conjunction with neuromuscular activation in individuals with HIV.

Conclusion

The objective of the present study was to assess the effects of tDCS on standing balance in PLHIV. Prior to this study and to the best of our knowledge, only one other study has investigated the use of tDCS treatment in an HIV population, thus warranting further investigation. The expansion of sway area and decline in balance performance may potentially contribute to an elevated risk of falling and frailty in elderly individuals with HIV. As a result, it is crucial to conduct thorough research on various interventions for balance and gait in this specific population in order to improve their quality of life and reduce the risk of falls and injuries. The findings of this study indicate that, tDCS could enhance standing balance in PLHIV. Furthermore, it is worth noting that there were no reported safety concerns or incidences throughout the present study. Hence, there will be no negative consequences if a clinician chooses to utilize tDCS for PLHIV.

The current study focused solely on the assessment of balance or a static activity, without taking into account any other factors or dynamic movements. Nonetheless, the protocol was derived from a prior study conducted by Rosario et al. [12], in which gait was examined. It is possible that subjects need more than five treatments to impact standing balance. Hence, it would be beneficial for future studies to explore additional treatment sessions and examine the impact of tDCS on functional outcome measures associated with balance and gait. It is also recommended that future research delves into the effectiveness of tDCS as a treatment option by conducting longitudinal studies over an extended period.

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Ethics approval: IRB approval TWU protocol # FY2020-32

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

Authors' contributions: All authors contributed to the study's conception and design.

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