Therapeutic effects of virtual reality video gaming on functional mobility, balance, and gait speed in individuals with tropical spastic paraparesis: A randomized crossover clinical trial

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Abstract

Introduction: Individuals with human T-cell lymphotropic virus 1-associated myelopathy/tropical spastic paraparesis (HAM/TSP) experience sensorimotor alterations, which can affect functional performance. Virtual reality (VR) videogaming is a therapeutic option, though there is scarce evidence for its use in this population. We aimed to investigate the therapeutic effects of a VR video game on functional mobility, balance, and gait speed in individuals with HAM/TSP. Methods: We conducted a blinded, crossover clinical trial comprising 29 individuals with HAM/TSP and randomized them into two groups: (1) early therapy: rehabilitative protocol started immediately after the initial evaluation and (2) late therapy: rehabilitative protocol started 10 weeks later. We assessed all participants for balance using the Berg Balance Scale (BBS) scores, functional mobility using the Timed Up and Go (TUG) test, and gait speed using video camera and CvMob software. Differences were considered significant if \( p < 0.05 \). Results: The early therapy group individuals presented with higher BBS scores \( (p=0.415) \), less TUG times \( (p=0.290) \), and greater gait speed \( (p=0.296) \) than the late therapy group individuals. Conclusions: VR videogaming is a useful option for rehabilitative therapy in individuals with HAM/TSP; it positively affects balance, functional mobility, and gait speed.

Keywords: Gait. Tropical spastic paraparesis. Mobility limitation. Postural balance. Virtual reality.

INTRODUCTION

Human T-cell lymphotropic virus 1 (HTLV-1)-associated myelopathy/tropical spastic paraparesis (HAM/TSP) is a neurological disorder characterized by demyelination of the central nervous system, predominantly the spinal cord\(^1\)-\(^5\). Initial signs of HAM/TSP include a reduction in muscular strength, lower-limb spasticity, and sphincter disorders\(^6\). This disease results in functional motor, sensory, and autonomic dysfunctions that lead to changes in gait, impaired balance, and loss of functional mobility, thereby increasing the risk of falling\(^1\)-\(^5\). Additionally, these physiological alterations may be influenced by fatigue arising from depressive symptoms as well as diminished social interactions, sense of well-being, and physical fitness\(^7\),\(^8\).

HTLV-1 infects an estimated 20 million people worldwide. In Brazil, this infection is endemic with the highest incidence reported in Salvador\(^9\), the capital of the northeastern state of Bahia. Secondary to HTLV-1 infection\(^10\), 3-5% of affected individuals develop HAM/TSP, with a higher prevalence in women aged \( \geq 40 \) years\(^6\),\(^9\). Nevertheless, HTLV-1 remains a neglected disease, and rehabilitation in HAM/TSP is crucial to promote functional improvement in affected individuals\(^4\),\(^11\),\(^12\).

Among the different rehabilitative strategies, studies have demonstrated virtual reality (VR) videogaming as a promising therapeutic option for motor and cognitive rehabilitation in patients with neurological impairments\(^13\),\(^14\), including demyelinating diseases such as HAM/TSP\(^13\),\(^15\),\(^16\) and multiple sclerosis\(^16\). However, evidence regarding the impact of VR in HAM/TSP rehabilitation
remains unclear. The present study aimed to investigate the effects of rehabilitation via VR videogaming on functional mobility, balance, and gait speed in HAM/TSP patients, considering the importance of these factors in fall prevention.

**METHODS**

The present randomized crossover clinical trial (ClinicalTrials.gov: NCT02877030) involved patients aged 18-64 years with independent gait, whose conditions were diagnosed as HAM/TSP according to the criteria of the World Health Organization. We excluded patients who were pregnant; presented with other neurological conditions, psychiatric disorders, rheumatic or orthopedic diseases; had previously undergone lower-limb amputation; or had difficulty in understanding the instruments used for the evaluation. This trial was part of a larger study approved by the local institutional review board (CAAE 49634815.2.0000.5628). All patients provided written informed consent.

In accordance with the CONSORT (http://www.consort-statement.org/) guidelines, a third party randomized the patients into two groups, late treatment (LT) group and early treatment (ET) group, using the online Random software (https://www.random.org/). Blinded and previously trained investigators evaluated the patients 10 and 20 weeks after the initial assessment, with a 1-week washout period after group crossover. For analysis, data from the LT group at the second assessment time point were used as controls for ET group, while ET data were used as controls for LT following the final assessment. Patients were asked to maintain their usual activities, including rehabilitation, throughout the evaluation time points.

Patients were evaluated for balance and functional mobility using the Berg Balance Scale (BBS) scores and the Timed Up and Go test (TUG), respectively. Habitual gait velocity was filmed using a GoPro HERO 3.0® camera and analyzed with CvMob software. In addition, patients answered a demographic questionnaire and provided a history of falls in the last 3 months, defined as “inadvertent fall to the ground or a lower level, excluding intentional changes in position using furniture, walls, or other objects as support.”

The ET group began the sensorimotor exercise protocol immediately after the initial assessment, whereas the LT group, considered as a control group for ET during this initial phase, initiated the protocol only at the beginning of the second 10-week study period. After this time point, the ET group received no therapeutic intervention, constituting the control phase. The ET and LT groups performed sensorimotor exercise sessions lasting 20 min, twice a week for 10 consecutive weeks: ET from weeks 1 to 10, and LT from weeks 10 to 20, following the 1-week washout period (Figure 1). We connected a VR videogame to a Nintendo Wii® console, in which arrows were randomly cast toward the player from above. Players were asked to move in the direction of the arrows to induce movements that displaced their body’s center of pressure using the Nintendo Wii® platform. Initially, arrows appeared at 3-s intervals, with a progressive increase in the appearance of arrows over the rehabilitation treatment period, demanding greater weight-shift from the participants. Patients who reported fatigue during a session were allowed to rest; resting periods were not deducted from the overall duration of 20 min per session.

Statistical analysis was performed using SPSS Statistics for Windows, version 17 (SPSS Inc., Chicago, IL, USA). The demographic and functional characteristics of participants were described with qualitative variables expressed using absolute and
TABLE 1: Demographic and functional characteristics of patients (N=29) with HAM/TSP.

| Variables                        | Total (N=29) | Early therapy (n=14) | Late therapy (n=15) | p value |
|----------------------------------|--------------|----------------------|---------------------|---------|
| Age in years (mean ± SD)         | 51.02±9.83   | 46.89±11.43          | 52.27±7.95          | 0.23    |
| Sex: Female n (%)                | 16 (55%)     | 9 (66.7%)            | 7 (45.5%)           | 0.40    |
| Use of walking aid, n (%)        | 15 (50%)     | 8 (55.6%)            | 7 (45.5%)           | 1.00    |
| History of falls, n (%)          |              |                      |                     |         |
| None                             | 4 (15%)      | 3 (22.2%)            | 1 (9.1%)            | 0.38    |
| One                              | 4 (15%)      | 0 (0.0%)             | 4 (27.3%)           | 0.38    |
| Two                              | 2 (5%)       | 1 (11.1%)            | 0 (0.0%)            | 0.38    |
| Three or more                    | 19 (65.0%)   | 10 (66.7%)           | 10 (63.6%)          | 0.38    |
| Berg Balance Scale score (mean ± SD) | 45.24±9.96 | 41.56±7.93          | 44.18±6.41          | 0.42    |
| Timed Up and Go - seconds (mean ± SD) | 17.44±11.29 | 22.19±12.72        | 18.13±6.87          | 0.37    |
| Gait speed - meters/seconds (mean ± SD) | 0.21±0.9   | 0.22±0.09           | 0.22±0.09           | 0.89    |

SD: standard deviation. *t-test; †Fisher’s exact test.

Comparisons between ET and LT interventions and control phases revealed a medium to large effect in functional mobility during the control phase. Patients in the LT group exhibited worse mean functional mobility scores than those in the ET group (Table 2).

DISCUSSION

Our results indicate a medium to large effect with regard to functional mobility, as assessed using TUG in the ET group. Studies have demonstrated that rehabilitation involving VR video games gradually provides greater freedom of movement to patients, who reportedly feel safer owing to less fear of falling and can interact physically with ease with their surroundings15,27-32. In addition, studies have reported that rehabilitative treatment for sensorimotor impairment contributed to increased adaptive plasticity33 and that repetitive practice was positively associated with motor learning34,13.

Differences between performance and motor learning have already been described, and some factors, including repetition and motivation, favor knowledge retention and the development of motor memory35. Moreover, VR treatment protocols vary greatly among studies30. In rehabilitation programs involving patients with multiple sclerosis, the total number of sessions was 10-3615,16, scheduled 1-3 times a week15,27, each lasting from 20-60 min27,32. A literature review identified only one clinical trial involving HAM/TSP patients, employing 30-min VR rehabilitation sessions scheduled three times a week over 8 weeks1.

Studies indicate that impaired balance in individuals with myelopathy results from reduced muscle strength35-39 and spasticity in the lower limbs2,35,36. In addition, sensory changes and associated brain injuries can further compromise postural38-43 and motor44 control, respectively. Notably, these sensory changes have been primarily associated with altered signal conduction through the ascending pathways in the thoracic spinal region, leading to reduced functional ability45. Memory consolidation and consequent motor learning are closely linked to motor and somatosensory information45.
The lower gait speed and inferior TUG performance seen in the LT group could be explained by the natural progression of myelopathy, which leads to impairment in gait and mobility, eventually necessitating the use of walking aids. Studies have linked functional mobility to several factors, including walking ability, weight transfer, balance, and muscle strength, all of which are impaired in individuals with HAM/TSP. Mobility presents as one of the greatest challenges for patients with HAM/TSP progression, and over 70% of the affected women report reduced mobility and locomotion. Gait speed was compromised in HAM/TSP patients, despite the use of walking aid devices.

Our results contribute to the body of knowledge surrounding the therapeutic effects of VR video games in the rehabilitation of patients with HAM/TSP. This study has its limitations. The most notable limitation is the small sample size, which is unfortunately common in studies involving this type of myelopathy. Moreover, considering disease progression and the possibility of loss to follow-up, it would be advisable to employ a longer washout time. It would also be interesting to account for the possibility of fatigue in affected individuals when planning session duration times; investigating pain levels could lend further insight.

The size effect of VR videogaming on functional mobility was medium to large exclusively in the HAM/TSP group that underwent rehabilitation therapy earlier in our study.

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AUTHORS’ CONTRIBUTION

EPF, KNS, RFRN, CRJS, MCMS, EBP: Conception and design of the study, Acquisition of data; Analysis and interpretation of data, Drafting the article, Final approval of the version to be submitted.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

REFERENCES

1. Coutinho IJ, Galvão-Castro B, Lima B, Eiter CCD, Grassi MFR. Impact of HTLV-associated myelopathy/Tropical spastic paraparesis (HAM/TSP) on activities of daily living (ADL) in HTLV-I infected patients. Acta Fisiátrica. 2011;18(1):6-10.
2. Champs APS, Passos VMA, Barreto SM, Vaz LS, Ribas JGR. Mielopatia associada ao HTLV-1: análise clínico epidemiológica em uma série de casos de 10 anos. Rev Soc Bras Med Trop. 2010;43(6):668-72.

3. Dias GAS, Yoshikawa GT, Koyama RVL, Fujihara S, Martins LCS, Medeiros R, et al. Neurological manifestations in individuals with HTLV-1-associated myelopathy/tropical spastic paraparesis in the Amazon. Spinal Cord. 2015;53(4):154-7.

4. Arnault VACO, Macêdo M, Pinto EB, Baptista AF, Castro-Filho BG, Sá KN. Virtual Reality Therapy in the treatment of HAM/TSP individuals: randomized clinical trial. Rev Pesq Fisio. 2014;4(2):99-106.

5. Moreno-Carvalho OA, Santos JI, Di Credico G. Evidence of preferential female prevalence of HTLV-1-associated tropical spastic paraparesis in Bahia-Brazil. Arq. Neuro-Psiquiatr. 1992;50(2):183-8.

6. Martin F, Fedina A, Youshya S, Taylor GP. A 15 years prospective longitudinal study of disease progression in patients with HTLV-1 associated myelopathy in the UK. J Neurol Neurosurg Psychiatry. 2010;81(12):1336-40.

7. Schwartz CE, Coulthard-Morris L, Zengi Q. Psychosocial Correlates of Fatigue in Multiple Sclerosis. Arch Phys Med Rehabil. 1996;77(2):165-70.

8. Colosimo C, Millefiorini E, Grasso MG, Vinci F, Fiorelli M, Koudravtseva T, et al. Fatigue in MS is associated with specific clinical features. Acta Neurol Scand. 1995;92(5):353-5.

9. Gallo RC, Willems L, Tagaya Y. Time to Go Back to the Original Name Frontiers in Microbiology. Front Microbiol. 2017;8:1800.

10. Gessain A, Cassar O. Epidemiological aspects and world distribution of HTLV-1 infection. Front Microbiol. 2012;3:1-23.

11. Sá KN, Macêdo MC, Andrade RP, Mendes SD, Martins JV, Baptista AF. Physiotherapy for human T-lymphotropic virus 1-associated myelopathy: review of the literature and future perspectives. J Multidiscip Healthc. 2015;8:117-25.

12. Neto IF, Mendonça RP, Nascimento CA, Mendes SM, Sá KN. Fortalecimento muscular em pacientes com HTLV-1 e sua influência no desempenho funcional: um estudo piloto [A pilot study: muscle strengthening in patients with HTLV-1 and its influence on functional performance]. Rev Pesq Fisio. 2012;2(2):143-55. Portuguese.

13. Holden MK. Virtual environments for motor rehabilitation: review. Cyberpsychol Behav. 2005;3(3):187-211.

14. Adamovich SV, Fluet GG, Tunik E, Merians AS. Sensorimotor training in virtual reality: a review. NeuroRehabilitation. 2009;25(1):29-49.

15. Lozano-Quilis JÁ, Gil-Gómez H, Gil-Gómez JÁ, Albiol-Pérez S, Koudriavtseva T, et al. Fatigue in MS is associated with specific clinical features. Acta Neurol Scand. 1995;92(5):353-5.

16. Eftekharsadat B, Babaei-Ghazani A, Mohammadzadeh M, Talebi M, Eslamian F, Ezari E. Effect of virtual reality-based balance training in multiple sclerosis. NeuroRehab. 2013;33(4):545-54.

17. World Health Organization (WHO). Human T lymphotropic virus type-1. Wkly Epidemiol Rec. 1988;64:382-383.

18. Borges JDP, Baptista AF, Santana N, Souza I, Kruschewsky RA, Galvão-Castro B, et al. Pilates exercises improve low back pain and quality of life in patients with HTLV-1 virus: a randomized crossover clinical trial. J Bodyw Mov Ther. 2014;18(1):68-74.

19. Miyamoto ST, Junior II, Berg KO, Ramos LR, Natour I. Brazilian version of the Berg balance scale. Braz J Med Biol Res. 2004;37(9):141-21.

20. Poshadiol D, Richardson S. The Timed "Up & Go": A Test of Basic Functional Mobility for Frail Elderly Persons. J Am Geriatr Soc. 1991;39(2):142-8.

21. Sebastião E, Sandroff BM, Learmonth YC, Motl RW. Validity of The Timed Up and Go as A Measure of Functional Mobility in Persons with Multiple Sclerosis. 2015; Arch Phys Med Rehabil. 2016;97(7):1072-7.

22. Fonseca EP, Sá KN, Nunes RFR, Ribeiro Junior AC, Lira SFB, Pinto EB. Balance, functional mobility, and fall occurrence in patients with human T-cell lymphotropic virus type-1-associated myelopathy/tropical spastic paraparesis: a cross-sectional study. Rev Soc Bras Med Trop. 2018;51(2):1-6.

23. Pena N, Credidio BC, Corrêa LPNRM, França LGS, Cunha MV, de Souza MC, et al. Instrumento livre para medidas de movimento. Rev Bras Ensino Fís. 2013;55(3):3505.

24. Quixadá AP, Onodera AN, Pena N, Miranda JGV, Sá KN. Validity and reliability of free software for bidimensional gait analysis. Rev Pesq Fisio. 2017;7(4):548-57.

25. Global report on falls prevention in older age. WHO Library Cataloguing-In-Publication Data ISBN 978 92 4 156353 6 (NLM classification: WA 288) World Health Organization 2007.

26. Rosenthal JA. Qualitative Descriptors of Strength of Association and Effect Size. Journal of Social Service Research. 1996;24(4):37-59.

27. Gutiérrez RO, del Rio FG, la Cuerda RC, Alguacil-Diego IM, Diego J, González RA. A telerehabilitation program by virtual reality-video games improves balance and postural control in multiple sclerosis patients. NeuroRehabilitation. 2013;33(4):545-54.

28. Nilsagard YE, Forsberg AS, von Koch L. Balance excise for person with multiple sclerosis using Wii games: a randomised, controlled multi-centre study. Mult Scler. 2012;19(2):209-16.

29. Massetti T, Trevican IL, Arab C, Favero FM, Ribeiro-Papa DC, Monteiro CBM. Virtual reality in multiple sclerosis - A systematic review. Mult Scler Relat Disord. 2016;8:107-12.

30. Baram Y, Miller A. Virtual reality cues for improvement of gait in patients with multiple sclerosis. Neurology. 2006;66(2):178-81.

31. Eftekharsadat B, Babaei A, Mohammadzadeh M, Talebi M, Eslamian F, Ezari E. Effect of virtual reality-based balance training in multiple sclerosis. NeuroRes. 2015;37(6):539-44.

32. Brichetto G, Spallarossa F, de Carvalho MLL, Battaglia MA. The effect of Nintendo Wii on balance in people with multiple sclerosis: a pilot randomizes control study. Mult Scler. 2013;19(9):1219-21.

33. Giotakos O, Tsirgogianni K, Tarnanas I. A virtual reality exposure therapy (VRET) scenario for the reduction of fear of falling and balance rehabilitation training of elder adults with hip fracture history. Conference: Virtual Rehabilitation 2007.

34. Levin MF, Weiss PL, Keshner EA. Emergence of virtual reality as a tool for upper limb rehabilitation: incorporation of motor control and motor learning principles. Phys Ther. 2015;95(3):415-25.

35. Shmuelof L, Krakauer JW, Mazzoni P. How is a motor skill learned? Changes and invariance at the levels of task success and trajectory control. J Neuropsychol. 2012;108(2):578-94.

36. Cantak SS, Winston CJ. Learning-performance distinction and memory processes for motor skills: A focused review and perspective. Behav Brain Res. 2012;228(1):219-31.

37. Cartier L, Araya F, Castillo JL, Ruiz F, Gormaz A, Tajima K. Progressive espatatic paraparesis associated with human T-cell leucemia virus type I (HTLV-I). Intern Med. 1992;31(11):1257-61.

38. Caiafa RC, Orsini M, Felicio LR, Puccionni-Shhler M. Muscular weakness represents the main limiting factor of walk, functional independence and quality of life of myelopathy patients associated to HTLV-1. Arq. Neuro-Psiquiatr. 2016;74(4):280-6.
39. Facchinetti LD, Araújo AQ, Chequer GL, de Azevedo MF, de Oliveira RVC, Lima MA. Falls in patients with HTLV-I-associated myelopathy/tropical spastic paraparesis (HAM/TSP). Spinal Cord. 2013;51(3):222-5.

40. Caskey MF, Morgan DJ, Porto AF, Giozza SP, Muniz AL, Orge GO, et al. Clinical manifestations associated with HTLV type I infection: a cross-sectional study. AIDS Res Hum Retroviruses. 2007;23(3):365-71.

41. Castillo JL, Cea JG, Verdugo RJ, Cartier L. Sensory dysfunction in HTLV-I-associated myelopathy/tropical spastic paraparesis. Eur Neurol. 1999;42(1):17-22.

42. Leite ACC, Silva MTT, Alamy AH, Afonso CRA, Lima MAD, Andrada-Serpa MJ, et al. Peripheral neuropathy in HTLV-I infected individuals without tropical spastic paraparesis/HTLV-I-associated myelopathy. J Neurol. 2004;251(7):877-81.

43. Facchinetti LD, Araújo AQ, Silva MTT, Leite ACC, Azevedo MF, Chequer GL, et al. Home-based exercise program in TSP/HAM individuals: a feasibility and effectiveness study. Arq. Neuro-Psiquiatr. 2017;75(4):221-7.

44. Moritoyo H, Arimura K, Arimura Y, Tokimura Y, Rosales R, Osame M. Study of lower limb somatosensory evoked potentials in 96 cases of HTLV-I-associated myelopathy/tropical spastic paraparesis. J Neurol Sci. 1996;138(1-2):78-81.

45. Araujo AQC, Silva MTT. The HTLV-1 neurological complex. Lancet Neurol. 2006;5(12):1068-76.

46. Cuppone AV, Semprini M, Konczak J. Consolidation of human somatosensory memory during motor learning. Behav Brain Res. 2018;347:184-92.

47. Vasconcelos BHB, Souza GS, Barroso TGCP, Silveira LCL, Sousa RCM, Callegari B, et al. Barefoot plantar pressure indicates progressive neurological damage in patients with human T-cell lymphotropic virus type 1 infection. Plos One. 2016;11(3):1-10.