STUDY PROTOCOL

Protocol for a controlled, randomized, blind, clinical trial to assess the effects of transcranial direct current stimulation associated with balance training using games in the postural balance of elderly people [version 1; peer review: 2 approved]

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Abstract
Aims: This study aims to evaluate the additional effect of transcranial direct current stimulation (tDCS) on training postural balance with the use of video games in aged.

Methods: This is a blinded, randomized, controlled clinical trial protocol, with elderly people of both genders. Participants will be randomized into three training groups: Group 1 (videogame balance training), group 2 (videogame balance training associated with active tDCS), group 3 (videogame balance training associated with sham tDCS). The training will be carried out twice a week for four weeks, totaling eight sessions, and will be performed with the Nintendo Wii videogame console, using games that stimulate the postural balance associated with tDCS, with anode applied over the left dorsolateral prefrontal cortex and cathode on the contralateral supraorbital region at 2 mA for 20 minutes. The postural balance will be assessed using the Mini Test of the Balance Assessment System and posturography. Evaluations will be carried out before and after eight training sessions and 30 days after the end of treatment.

Discussion: Some studies show favorable results from the use of video games in improving postural balance in the elderly; however, their effect does not remain long-term. TDCS associated with other therapies can potentiate and prolong the effects of these therapies owing to its ability to stimulate neurotrophins important for neurogenesis, facilitating tasks that require attention, and helping to consolidate learning and memory. The effect of the two associated techniques on balance have not yet been tested in this population.

Registration: Brazilian Registry of Clinical Trials ID U1111-1213-4266; registered on 15 October, 2018.
Keywords
Elderly, postural balance, transcranial direct current stimulation, video game

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Author roles: Kunitake AI: Conceptualization, Methodology, Project Administration, Supervision, Validation, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing; Corrêa JCF: Funding Acquisition, Resources, Software; Nascimento KS: Investigation, Project Administration, Supervision; Oliveira BBCd: Investigation, Project Administration, Supervision; Muniz NM: Investigation, Project Administration, Supervision; Silva SM: Data Curation, Formal Analysis, Validation; Corrêa FI: Conceptualization, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

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Introduction
Aging is a physiological occurrence that has several consequences, including an increased risk of falls. The incidence of falls increases proportionally to age, from 28% to 35% in the elderly over 65 years and from 32% to 42% in those over 75 years. Falls can lead to musculoskeletal injuries, and in more severe cases, they can lead to death.

Preventive therapies for the risk of falls can be performed with the use of technological resources, such as videogames. Studies using videogames have shown positive effects in improving the postural control, balance, and functional capacity of the elderly when practiced regularly. They have been widely used by therapists with high acceptance in clinical practice because they are motivating, challenging, and recreational, showing good evidence to improve postural control in the elderly.

Another technique that has aroused interest in clinical practice is transcranial direct current stimulation (tDCS), which consists of low-intensity current, and can be applied to the scalp by means of rubber electrodes, thus promoting changes in the potential of resting membrane, such as depolarization by the anode electrode or hyperpolarization by the cathode; modulating cortical excitability. Anodic tDCS, when applied over the long term, can stimulate the brain-derived neurotrophic factor (BDNF), which is an important protein for stimulating neuroplasticity, improving attention, consolidating learning, and memory. Thus, its use has aroused interest for the elderly, in order to reduce cognitive and motor declines.

However, the protocols for the use of tDCS associated with tasks that involve balance, in order to improve balance are not yet defined, and are being applied in different dosages and locations, therefore, further studies are necessary to verify the benefit of tDCS in association with other therapies. For that reason, the objective of this study is to assess whether tDCS can enhance and prolong the effects of videogame training on improving postural balance in the elderly. This study hypothesizes that the association of tDCS with virtual reality therapy is more effective in improving balance in the elderly than therapy with videogames alone, and that the addition of tDCS will prolong the effects of balance training.

Methods
Study design
This is a protocol for a randomized, controlled blind, longitudinal clinical trial, as shown in Figure 1. This project will be carried out at University Nove de Julho in São Paulo, Brazil.
Eligibility criteria
The inclusion criteria are people between 60 and 80 years old, of both genders, able to stand or walk without the aid of auxiliary devices, with reduced balance (score ≤ 25 points) evaluated using the Mini-BESTest\(^7\). Exclusion criteria are cognitive impairment (scores ≤ 14 points) corrected for education, measured by the Mini-Mental State Examination (MMSE)\(^8\), presence of lower limb fractures or amputations, neurological diseases, cardiovascular diseases that limit the performance of exercises, untreated acute and chronic respiratory diseases and the presence of pain that limits movement; the presence of contraindications to the use of tDCS.

Consent to participate
The informed consent form will be explained to all participants. The volunteers who participate in this study, must sign the form (supplementary file 1), which guarantees the secrecy and confidentiality of data, free access to the final data, explanations of any kind related to the study and possible compensation for those that suffer from participation in the study.

Ethics approval
The protocol was approved in May 2018 by Human Research Ethics Committee of the University Nove de Julho, São Paulo, Brazil (Opinion number 2.962.837), and Brazilian Clinical Trials Registry (ReBec), number: U1111-1213-4266, in accordance with Resolution 466/12 of the National Health Council of Brazil.

Recruitment and allocation
Participants in this study will be community elders elected according to the criteria established for allocation. They will be randomized into 3 groups:

- Group 1: Control Group (Balance training with video game);
- Group 2: Active group (balance training with video games associated with active tDCS);
- Group 3: Sham Group (Balance training with video games associated with sham tDCS).

A researcher not involved in evaluations or training will be responsible for allocating participants via [www.randomization.com](http://www.randomization.com).

Sample size
The sample size was obtained using G\(^*\)Power 3.0.10 software, based on the outcomes from a pilot study. The calculation was carried out by the two-way repeated measures analysis of variance (ANOVA), considering the mean value (before and after training, and 30-day follow-up) for the control groups (25.46) active (27.46) and sham (24.66) and the pooled standard deviation (SD\(_{pooled}\)) (2.89), with \(\alpha = 0.05\), \(\beta = 0.2\) (80% of power) and the effect size of 0.40. A total of 15 individuals were determined to be required for each group (total sample: 45 individuals). Considering possible dropouts and to ensure a sample size that will demonstrate the effect of the intervention, the sample will be expanded by 25%, resulting in 19 individuals in each group, thus totalling 54 participants.

Outcome assessments
All evaluations will be carried out on three occasions: pre-intervention, after eight treatment sessions and 30 days after the end of the training (follow-up). The training will be held twice a week, for 4 weeks, totalling 8 sessions.

Postural balance. The assessment of postural balance will be performed by the Mini BESTest Scale, which consists of 14 functional tasks, such as sitting and getting up from a chair, standing up, balancing on tiptoes, and on one foot, overcoming walking obstacles, and double activities task\(^2\).

Performance can range from 0 to 28 points. Each test can be performed for up to three attempts and the best result will be obtained. If adaptations are necessary to accomplish this, a point will be deducted from the maximum score obtained. This is a very reliable instrument, with an intraclass correlation (ICC) of 0.84\(^3\).

Static postural balance. Posturography data will be collected using the Wii Balance Board (Nintendo, Kyoto, Japan), which is a validated instrument for posturography evaluation\(^4\). The software for postural assessment is available at [http://www.rehabtools.org/sway.html](http://www.rehabtools.org/sway.html).

The evaluation protocol will be performed in two conditions, standing with eyes open and then with eyes closed. These two postures are reliable for measuring body sway, with eyes open with (ICC: 0.77) and with eyes closed (ICC: 0.89)\(^5\).

To standardize the collections, the initial position of the feet on the evaluation platform will be marked and the same measurement repeated in all evaluations. The tests will last 1 minute, the initial 30 seconds will be to establish the patient’s suitability and the final 30 seconds will be to collect the posturography data.

Potential confusion factors
Symptoms of depression. The symptoms of depression will be evaluated and classified according to severity, using the Beck Depression Inventory (BDI), a questionnaire composed of 21 questions, which can be self-applied. Scores from 0 to 10 indicate an absence of depression; 11 to 18 indicate mild depression; 19 to 29 indicate moderate depression and 30 to 63 is considered severe depression\(^6\). In studies with the elderly, the BDI score shows a degree of reliability \(r = 0.78\)^\(^7\). Subsequently, it will be assessed whether the emotional state interfered with the results.

Quality of life (QOL). QOL will be measured by the World Health Organization’s Quality of Life Instrument, Bref version\(^8\), which is composed of 26 questions, scored from 1 to 5, with the worst and the best scores being 26 and 130, respectively. In studies with the elderly, it showed a high degree of reliability.
to mediate quality of life in the domain of physical capacity (0.89), psychological well-being (0.95), social relationships (0.81), and the environment (0.93).

The use of medication
The information related to continuous-use medication will be monitored through the application of a questionnaire prepared by the author. Such information will be used to characterize the sample.

Intervention procedures
Balance training with video games. The balance training sessions will be performed using only the video games in group 1 (control), group 2 will be the balance training with the video games associated with the active tDCS and group 3 will be the balance training with the video games associated with the tDCS sham.

Video game training will be carried out with the Nintendo Wii and Wii Fit Plus, placed in a slide projector to enlarge the image. The sequence of games will always be the same, and the participant should play an average of 5 to 7 minutes each game, passing the stage according to their learning.

The sessions will be held twice a week, for four weeks, totalling eight sessions. Each session will last 20 minutes. The selected games are table tilt, penguin slide and ski slalom, which will be performed standing on the Wii Board Balance and require movements that stimulate balance, such as the anterior, posterior and lateral tilt of the body, without moving (Figure 1).

tDCS

The intensity will be 2mA with a 20-second ramp up and down for a 20-minute period of stimulation. The montage will be anodal, unbalanced bilateral bipolar, anode positioned over the dorsolateral prefrontal cortex of the dominant hemisphere (F3 or F4) and the cathode electrode on the supraorbital region contralateral to the anode (Figure 2), according to the criteria of the 10–20 electroencephalogram system.

Assessment of the potential adverse effects
At the end of each session, a questionnaire on the adverse effects of tDCS will be applied to the participant (see Extended data, Assessment of ETCC Adverse Events form).

Blinding
The NeuroConn DC-STIMULATOR PLUS device has settings that allow the selection of the active stimulation or sham mode, by inserting codes. A researcher not involved in the procedures will program the equipment with the code to which the individual will be allocated. The stimulus mode will not be perceived by the external (supplementary functioning of the device, therefore, neither the researcher who will apply the intervention nor the individual will know what treatment will be applied (double-blind).

Participants in the group that will only perform training with videogames will not be blind to treatment; however, a researcher will be responsible for the exclusive training of this group and will not be aware of the procedures with the tDCS of the other groups. All assessments will be made by researchers who have not participated in the training of the elderly, and will, therefore, be blind to the intervention. A blinding questionnaire will be applied to guarantee its reliability and satisfaction with the treatment received (supplementary files 3 and 4), without the researcher knowing the training carried out by the participant.

Statistical analysis
All statistical tests will be performed using SPSS (V22, IBM Corporation, New York, USA). Initially, we will perform the test of normality of the sample using the Shapiro-Wilk
test, considering the significance level defined as a value of \( \alpha < 0.05 \). The parametric data will be expressed as a mean ± SD (standard deviation), and the nonparametric data as a median (IQR); the categorical data will be described as absolute values and as a percentage of the total sample.

The variables of the data of the Mini-BESTest, Posturography, obtained pre-intervention, post-intervention and 30-day follow-up for the three groups (control, active and sham) will be calculated by the two-way repeated measures analysis of variance (ANOVA) for the parametric data and the Friedman’s test for the nonparametric data.

Finally, to verify whether there is a correlation between BESTest values and the symptoms of depression and quality of life, Pearson’s R correlation (parametric) or Spearman correlation (nonparametric) for the three groups in three evaluated times will be performed, verifying the degree of correlation (r) and its significance (p).

Trial status
The protocol was approved in May 2018 by the Brazilian Clinical Trials Registry (ReBec) U1111-1213-4266. Submission of the manuscript occurred after this period, with the collection taking place and the completion is expected to happen in December 2020. The outcomes of this study will be subsequently published in a journal of interest.

Discussion
The incidence of falls has become an aggravating problem with the increase in the number of elderly people and life expectancy. The costs of falling are also high; prevention is an effective and inexpensive alternative when compared to any other procedure\(^{28,29}\).

Preventive therapies can be performed with the use of video games, since they can be used to improve postural control and balance in the elderly, helping to prevent falls. Besides, they are well accepted for being motivating and recreational and can be easily performed at home\(^{7-10}\).

However, there are several types of training protocols, which can vary from 4 to 20 weeks\(^{22}\). For some elderly people, this long process of therapy can be tiring; however, for the consolidation of learning and memory to occur, repetitive training is necessary. According to\(^{29}\), the learning and memory process is directly related to the number of repetitions performed by the elderly, with a better effect in the long run. In this sense, the simultaneous application of tDCS can be a resource that can assist in this process of consolidating learning, improving attention for its ability to stimulate neuroplasticity. For the elderly, it can be an important tool in the rehabilitation process, as it is known that, with advancing age, they present cognitive and motor decline\(^{11-14}\).

However, one of the limitations of using tDCS for the elderly is that few studies have investigated its effects on this population; some showing positive effects\(^{16,18,30,31}\), while others do not\(^{17,32,33}\). Protocols combining the two resources have already been carried out in children with cerebral palsy\(^{34}\), Parkinson’s disease\(^{35}\), spinal cord injury\(^{19}\) and stroke victims\(^{37,38}\). However, studies that associated tDCS and video games in the elderly was not found.

Conclusion
This article presents a randomized, controlled and blind protocol developed to show the effect of the combination of transcranial direct current stimulation (tDCS) associated with training using video games in the elderly. The outcomes obtained will be published and their evidences may contribute for new training alternatives in the elderly.

Data availability
Underlying data
No underlying data are associated with this article.

Extended data
Harvard Dataverse: A PROTOCOL OF A CONTROLLED, RANDOMIZED, BLIND, CLINICAL TRIAL, TO CHECK THE EFFECTS OF TRANSCRANIAL DIRECT CURRENT STIMULATION (tDCS) ASSOCIATED WITH BALANCE TRAINING USING GAMES IN THE POSTURAL BALANCE OF ELDERLY PEOPLE. https://doi.org/10.7910/DVN/OJBWHJ

File ‘Suplementary File.docx’ contains the following extended data:
- Model informed consent form.
- Assessment of ETCC Adverse Events form.
- Blinding questionnaire.
- Satisfaction questionnaire.

Reporting guidelines
Harvard Dataverse: SPIRIT checklist for ‘Protocol for a controlled, randomized, blind, clinical trial to assess the effects of transcranial direct current stimulation associated with balance training using games in the postural balance of elderly people’. https://doi.org/10.7910/DVN/OJBWHJ

Data are available under the terms of the Creative Commons Zero “No rights reserved” data waiver (CC0 1.0 Public domain dedication).

Acknowledgments
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This interesting ongoing randomized controlled trial examines whether anodal tDCS applied over the dorsolateral prefrontal cortex can enhance and/or prolong the effects of videogame training on balance in older adults. The authors report existing approval by the local ethics committee and ongoing training/intervention and data collection. The study is registered at ensaiosclinicos.gov.br. Methods are sound. I have only a few suggestions that I believe will make the manuscript clearer.

- Please mention stimulation type (i.e., "anodal" or "anodic") and targeted area (i.e., dorsolateral prefrontal cortex) in the title and aims (abstract and main text).
- Please clarify why the study includes a "control group" (no electrodes positioning) and a "sham group" (placebo tDCS).
- Please provide further details about the sham tDCS (e.g., will any current intensity be applied? For how long? Etc.)
- Please avoid the use of “elderly”. Consider using “older adults/people” throughout the entire manuscript.
- The primary/secondary outcome measures should be explicitly identified.

**Is the rationale for, and objectives of, the study clearly described?**
Yes

**Is the study design appropriate for the research question?**
Yes

**Are sufficient details of the methods provided to allow replication by others?**
Yes

**Are the datasets clearly presented in a useable and accessible format?**
Not applicable

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Movement Science and Neuroscience, with experience in conducting clinical trials and reporting their findings.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

[Reviewer Report 02 November 2020](https://doi.org/10.5256/f1000research.27770.r71407)

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[✔] **Fernando Zanela da Silva Arêas**
Center of Health Sciences, Discipline of Physical Therapy, Federal University of Espírito Santo (UFES), Vitória, Brazil

The paper is well delineated, and well written - it is clear, objective and relevant. The protocols follow all the ethics criteria for reproduction. Also, the literature does not have works that investigate the approach with this methodologic quality.

Does the project have some finance?

This is a good project. I recommend indexing.

**Is the rationale for, and objectives of, the study clearly described?**
Yes

**Is the study design appropriate for the research question?**
Yes

**Are sufficient details of the methods provided to allow replication by others?**
Yes

**Are the datasets clearly presented in a useable and accessible format?**
Yes

**Competing Interests:** No competing interests were disclosed.
Reviewer Expertise: Neurorehabilitation, neuromodulation, traumatic brain injury

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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