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Effects of exergames training on Postural Balance in chronic stroke patients: study protocol for a randomized controlled trial

Nathalia Priscilla Oliveira Silva Bessa[1]; Bartolomeu Fagundes de Lima Filho[1]; Candice Simões Pimenta de Medeiros[1]; Tatiana Souza Ribeiro[1]; Tânia Fernandes Campos[1]; Fabricia Azevedo da Costa Cavalcanti[1].

[1] Departament of Physical Therapy, Federal University of Rio Grande do Norte, Natal, Brazil.

*Corresponding author: Nathalia Priscilla Oliveira Silva Bessa. Laboratory of Virtual Reality, Departament of Physical Therapy, Federal University of Rio Grande do Norte, Senador Salgado Filho Av, 3000, Natal, Rio Grande do Norte, Brazil. Email: nathyzinhasilva@gmail.com

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Abstract

Introduction: Exergames training, as an additional therapy to standard care, has been widely used for motor recovery after stroke. However, there is insufficient evidence to reach conclusions about the isolated effectiveness of exergames on gait speed, balance, and the quality of life compared to that of traditional rehabilitation training. The study describes a single-blind randomized clinical trial that aim is to investigate the effects of exergames training on postural balance in patients with chronic stroke.

Methods and analysis: Forty-two individuals with chronic stroke (> 6 months), aged from 20 to 75 years, will be randomized into two groups: experimental group, which will be submitted to an exergames protocol and control group which will undergo kinesiotherapy protocol, both protocols are based on postural balance. The intervention will consist of 40-minute sessions twice a week for 10 consecutive weeks. The volunteers will be evaluated before the treatment, at the end of the interventions and 8 weeks after. The primary outcome will be postural balance, and secondary outcomes will be gait, cortical activation patterns, functional independence, quality of life, and motivation.

Ethics and dissemination: This protocol has been approved by the Ethics Committee of Federal University of Rio Grande do Norte (number: 3.434.350). The results of the study will be disseminated to participants through social networks and will be submitted to a peer-reviewed journal and scientific meetings.

Trial registration number : RBR-78v9hx (Brazilian Registry of Clinical Trials – ReBEC).

Keywords: Stroke, Randomised Controlled Trial, Postural balance, Rehabilitation, Physical therapy modalities, Virtual Reality Exposure Therapy.

Strengths and limitations of this study

- This study will be explore objective data of the postural balance and gait through the force platform and kinematic analysis;
- This study is among the few that use EEG to assess brain activity in stroke individuals undergoing in an experimental protocol with exergames;
- The results of this research can lead to enhancements about how to improve the use of exergames for postural balance in the stroke rehabilitation;
- This study should benefit participants not only in physical aspects but also in psychological and social aspects;
- The blinding of participants will be not possible because the nature of the intervention;

Introduction

According to the World Health Organization, cerebrovascular disease was the leading cause of death worldwide in 2016. Of those deaths, 5.78 million were directly attributed to stroke, making it the main non-communicable cause of death[1]. In Brazil, stroke resulted in approximate 100,000 deaths in 2014[2], and data indicate that about 568,000 affected individuals suffer from severe disability, making stroke the leading cause of disability in adults[3].

Following stroke, various aspects of balance function are altered, such as delay in regaining the ability to assume the standing posture, loss of balance, asymmetry between the right and left limbs, increased posture sway, and decreased weight bearing on the affected side[4,5]. Postural balance is important for functional tasks such as sitting, sit-to-stand, and walking, and dysfunction leads to alterations in weight distribution patterns, causing the paretic leg to take less load[6]. These changes promote high risk of falling, difficulties in executing functional activities and reduced performance of daily living activities, and a consequent reduction in social participation which can aggravate the clinical situation[7].

Underuse of the impaired limb results in suppression of the cortical representation of the affected limb and further inhibition of its use[8]. The existence of cortical neural resources specialized in capturing changes in postural stability, which have been detected by changes in electroencephalography (EEG), support the idea that postural adjustments are not only due to muscle responses to disorders but also due to cortically controlled intentional movements that may be altered following stroke[9].

One major component of stroke rehabilitation is exercise therapy[10] and motor skill learning is particularly attractive since practice-induced improvement of sensorimotor performance supports the development of new aptitudes, providing the flexibility to adapt to changing conditions[11].

These perspective, virtual reality (VR)-based exercises, also known as exergames, have been widely used in rehabilitation with the aim of improving sensorial, cognitive, psychological, and motor function[12,13]. They have been characterized as an experience that simulates a real environment in which the user can interact with the scenario created by the game through the involvement of multisensory aspects[14]. Exergames applications have the potential to apply relevant concepts of neuroplasticity, such as repetition, intensity, and task-oriented training of the paretic extremity[7], and may entrain several brain areas involved in motor planning and learning, thus leading to an enhanced motor performance in rehabilitation[12,15,16].

There is some evidence to suggest the effectiveness of exergames in improving upper limb function and balance as an additional therapy to standard care in stroke patients. However, there is insufficient evidence to reach conclusions about the isolated effectiveness of exergames on gait speed, balance, participation, or the quality of life compared to that of traditional rehabilitation training [17,18].

A meta-analysis by Lee *et al.* (2019) found moderate evidence to support the effect of exergames training on improved lower limb function, including balance and gait, to a similar degree as upper limb function in chronic stroke patients, suggesting that this technique may be used as a complementary treatment method alongside traditional rehabilitation therapy. However, most of

the studies in this meta-analysis increased the overall treatment time by adding exergames training to conventional treatment, and this may be the reason for the observed outcomes[19].

Considering the above evidence, it is paramount to investigate the isolated effectiveness of exergames rehabilitation and its contributions to positive changes in postural balance in stroke patients as this may provide additional evidence for the rehabilitation process in this population. The proposal of the study is to investigate the effects of exergames training on postural balance in patients with chronic stroke and to explore changes in cortical activation patterns, functionality, quality of life, and motivation.

Methods and Analysis

Design

A single-blind randomized controlled clinical trial that follows the recommendations of the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)[20] (Figure 1) . Participants will be randomised to receive exergames protocol (experimental group - EG) and kinesiotherapy protocol (control group - CG) (Figure 2).

[INSERT Image 1]
[INSERT Image 2]

Participants

The study population will consist of forty-two chronic stroke patients who live in the city of Natal or nearby. A volunteer selection will be carried out in stroke patient care centers in the city. The selection can also be carried out via spontaneous demand by the voluntary search of stroke patients after project

advertisement on social media. After this, the first telephone contact will be made to clarify any questions from the participants, and the first screening for inclusion will be performed.

Inclusion and exclusion criteria

The participants will be selected according to the following criteria: (1) first episode of unilateral stroke (ischemic or hemorrhagic); (2) postural balance deficits (Berg Balance Scale score -BBS) <45)[21]; (3) injury time ≥6 months; (4) age between 20 and 75 years; (5) at maximum level 2 of the modified Ashworth Scale to assess the spasticity of the paretic lower limb[22]; (6) good cognitive status based on the Mini-Mental State Examination (MMSE)[23]; (7) ability to walk without personal assistance indoors (Functional Ambulation Category -FAC) scores ≥3)[24]; (8) clinically stable, with no history of epilepsy or seizures in the last 6 months; (9) not having signs of unilateral neglect or sensory or global aphasia as assessed by National Institute Health Stroke Scale -NIHSS)[25]; (10) no uncorrected hearing and/or visual impairments; (11) not participating in a balance treatment protocol; and (12) ability to understand and obey simple motor commands.

Exclusion criteria will include (1) presenting other clinical conditions affecting balance and (2) pregnancy.

Sample Size

Using an online calculator[26] and based on previous study values (51.0±4.6 and 46.2±5.7)[27] a total sample of participants 42 (21 in EG and 21 in CG) will be sufficient to detect a clinically important difference between the

groups on the BBS. A statistical power of 80% and an alpha of 5% and a loss rate of 10% were considered for the sample calculation.

Randomization and blinding

A randomization sequence will be generated by a computer[28] in 3 blocks of 12 participants and 1 block of 6 participants, allowing participants to be equally distributed between the 2 groups. This stage will be conducted by a researcher, not involved in the study, which will keep the randomization list confidential until the end of the study and will organize the allocation in sequentially numbered opaque envelopes. These envelopes will be sealed, and the randomization sequence will be enforced using color coding for the study groups (blue and red) that will correspond to the protocol that will be executed. The contents of each envelope will be revealed at the beginning of each patient's training by the study therapists responsible for the intervention to maintain allocation confidentiality. The same therapists involved in CG training will perform training in the EG. The researcher responsible for evaluations will be blinded to all intervention groups. The only variables that will be collected during the training will be evaluated by study therapists (non-blind). Statistical analysis will be performed by a blind researcher who will treat the groups according to color and the equivalence between groups and colors will be revealed upon completion of the statistical analysis. The main researcher (assessment) will have access to the final trial dataset; this researcher will decide terminate the trial. All information about participants will be confidentiality before, during and after the trial.

Evaluation procedures

The researchers will be trained before data collection procedures to ensure the reliability of measurements and the participants will be submitted to assessment using all the instruments mentioned bellow.

Measures

Sample characterization measures

- Cognition: MMSE is a validated instrument in Brazil to assess cognitive function. The total score ranges from 0 to 30 points, and the higher the score, the better the cognitive ability, according to education. Good cognitive status is considered with scores equal to or higher than 24 points for literate persons and 19 for illiterate persons[23].
- Ability to walk: This will be evaluated by the FAC which is a sensitive and reliable instrument for gait evaluation in stroke patients with hemiparesis[24] and ranks the ability to walk according to the amount of physical support required for the task. The score can vary from 0 (unable to walk or needs the help of 2 therapists) to 5 (independent in locomotion).
- Spasticity: The modified Ashworth scale allows subjective assessment of muscle tone and classifies the affected segments from 0 (normal tone) to 5 (rigid affected part)[22].
- Clinical and demographic data: Personal information, anthropometric data, demographic partner and pathological (injury time, paretic side, stroke type) and clinical history (history of falls, physical therapy treatment, and previous use of exergames) will be collected.

- Neurological impairment: NIHSS is a specific instrument to assess the severity of stroke via 10 items and is reported to have excellent validity and reliability[25].

Outcome measures

Primary outcome measures considered for this study are as follows:

Postural Balance:

- Berg Balance Scale: BBS is a valid and reliable instrument for measuring both the static and dynamic aspects of balance in people after stroke. BBS scores range from 0 to 56, and values below 45 points are predictive of falls, indicating a significant change in balance[21,29]. In the present study, test scores with the paretic limb positioned behind will be used in item 13 and unipodal support over the paretic limb will be used in item 14, minimizing the ceiling effect in individuals with better balance[30].
- Functional Reach Test (FRT): FRT assesses a patient's stability by measuring the maximum distance an individual can reach forward while standing in a fixed position, as is widely used to identify the risk of falling[31]. Displacements < 15 cm indicate patient fragility and risk of falls[32].
- Timed up and Go test (TUG): It is a valid instrument for assessing mobility and functional balance involving power, speed, and agility[33]. Performing the test within 10 seconds is considered normal for healthy, independent adults without the risk of falls. Values from 11 to 20 seconds are expected for disabled or frail elderly people with partial independence

and a low risk of falls. Values > 20 seconds suggests that the elderly have significant physical mobility deficits and risk of falls[34].

- Centre of Pressure variables (CoP): Data for total displacement, anteroposterior, and midlateral velocity of the CoP will be assessed using the gold standard equipment for balance assessment, the force platform (FP)[35]. The Bertec® model 4060 connected to an external amplifier (Bertec® AM651X) will be used.

The following secondary outcome measures are considered for this study:

Cortical Activation Pattern

Alpha and beta frequencies will be evaluated due to their relationship with the motor learning process[36], using the Emotiv EPOC®, portable 14 sensor electroencephalography (EEG) device, gyroscope capable of detecting changes in the movement performed.

Gait kinematic analysis

The spatiotemporal and angular gait variables will be evaluated by the 6-m timed walk test and Kinovea® software.

- Six-Meter Timed Walk (6MTW): It is a valid and reliable test for the assessment of the walking ability of patients with stroke[37]. Gait speed should be self-selected and considered comfortable and usual for the participant. Studies show variation in mean habitual speed (0.45 m/s - 0.78 m/s) of gait in individuals with hemiparesis[38,39].

- Software Kinovea®*:* Kinematic evaluation will be performed during gait video capture (6MTW) using the Sony DCR-DVD850 digital cam, 2.7/6.7 cm LCD screen, 60x optical zoom. Data will later be exported to Kinovea® 0.8.15 software for paretic lower limb angle and gait speed analysis. This is public domain video editing and analysis software that is valid, reliable, and capable of accurately measuring distances up to 5 meters from the object[40].

Functional independence

The Functional Independence Measure (FIM) scale will be used due to its reliability, validity, precision, and feasibility criteria. It is composed of 18 items including motor and cognitive items, in a system where the patient's answers graduates from 1 (total dependent) to 7 (complete independence) and the total punctuation ranges between 18 and 126. For this research, the FIM will be applied exclusively to the motor items, limiting the minimum score to 13 and the maximum to 91 points[41].

Quality of life

The assessment of quality-of-life perception will be performed through a quality-of-life assessment scale in stroke (Stroke-Specific Quality of Life Scale [SS-QoL]). It is valid and reliable in assessing the quality of life after stroke in the Brazilian population and has 49 items distributed over 12 domains[42].

Motivation

Intrinsic Motivation Inventory (IMI) is a multidimensional measurement with 6 subscales used to assess the subjective experiences of participants when developing an activity and attends to the reliability, validity criteria. According to the inventory, instruction participants ranked their agreement with each statement on a Likert scale of 1 ("not at all true") to 7 ("very true")[43].

Participant monitoring measures

Participants will be monitored during interventions by the following measures:

- Cardiovascular parameter variables: Heart rate (HR) will be checked by portable oximeter and Blood pressure (BP) by sphygmomanometer (Visomat Comfort III®, Incoterm, São Paulo, Brazil) on the non-paretic arm.
- Adverse symptoms, perceived effort, and pain: Information regarding headache, vomiting, and dizziness will be collected. Quantification of perceived effort and pain will be used as indicators to monitor exercise tolerance through the CR-10 (Category-Ratio Scale) Borg Scale[44] modified by Foster *et al*. [45] (2001).

Adverse events

Additional information such as hospitalizations, falls, out-of-routine medical consultation, medication change, new diagnosis, and presence of negative event will be collected during the follow-up.

Interventions

The protocols in both groups will be performed individually through 40-minute sessions twice a week for 10 weeks (total of 20 sessions), totaling 13

hours of intervention[12,17,46]. The same outcome measures and motivation will be collected again at the end of the interventions (post-training) and after 8 weeks of the end of the interventions (follow-up). All participants will be instructed not to perform any other physical activity that works on body balance during the study period.

During each session, the absences, manifestations of adverse symptoms, and occurrence of imbalance and/or falls will be recorded. Interventions modifications will be performed according patient's level of adaptation involving optimization of time or number of repetitions; and/or rest time enlargement and all will be registered.

Both groups will begin their protocols with adapted lower limb strength training for 10 minutes[47,48] as described in Table 1. Each exercise should be performed with respect to the patient's level of adaptation and evolution will occur in the 6th and 13th sessions using the materials described.

Table 1. Lower limb strengthening exercises.

Exercise	Evolution	Materials Used	Sets
1. Get up and sit on a chair	Surface change	1 or 2 mats to create an unstable surface (H: 3 x W: 43 x L: 93 cm).	2 sets of 60 seconds with 30 seconds of rest
2. Go up and down steps	Increase the step height; add weight	Larger step and 1 kg shin pad.	
3. Strengthening of hip extensors	Add weight	1 kg and 2 kg shin pad.	
4. Tiptoe rise	Add weight	1 kg and 2 kg shin pad.	

Source: adapted from Allet et al. (2010).

Control Group

Participants in the CG will receive a kinesiotherapy protocol (30 minutes) (Table 2) focusing on balance based on previous studies and promotes stimuli similar to the EG and were selected so that they demand identical motor sensors in both intervention environments, real and virtual[47-50]. Two progressions will happen, respectively, in the 6th and 13th sessions.

Table 2. Kinesiotherapeutic protocol exercises.

Exercise	Evolution	Materials Used	Sets**
1. Gait training on a stable surface.	Gait training on an unstable surface using mats; addition of shin pads of 1 kg.	Mat* and 1 kg shin pads.	2 sets of 3 minutes
2. Laterolateral weight transfer and discharge.	Addition of 1 and 2 mats respectively.	Mat	3 sets of 60 seconds
3. Anteroposterior weight transfer and discharge.	Addition of 1 and 2 mats respectively.	Mat	3 sets of 60 seconds
4. Laterolateral cephalic movement with eyes open.	Same movement with eyes closed. Added an exercise mat.	Mat	3 sets of 60 seconds
5. Anteroposterior cephalic movement with eyes open.	Same movement with eyes closed. Added an exercise mat.	Mat	3 sets of 60 seconds
6. Dissociation of scapular and pelvic girdles.	Addition of 1 and 2 mats respectively.	Mat	3 sets of 2 minutes

Source: Adapted from Nascimento, Patrizzi, Oliveira (2012); Soares, Sachelli (2008); Allet et al. (2010) e Ribeiro (2015). Legend: *The mats (height: 3 x width: 43 x length: 93 cm) will be used to create an unstable surface; **For each series performed, the participant will be entitled to 30 seconds of rest.

Experimental Group

Participants in the EG will receive a seven Wii Fit Plus exergames on the Nintendo Wii® (30 minutes) (Table 3). This will use the Wii Balance Board (WBB) accessory, a multimedia projector, the Wii Remote Controller and

initially, participants will have a moment to adapt to Nintendo Wii and its components.

Table 3. Exergames protocol exercises.

Game	Description	Progression
1. Free Run	Control in patient's pocket "marching" on firm surface	Addition of 1 and 2 mats* respectively
2. Soccer Heading	On WBB; performs anteroposterior and laterolateral weight transfer to virtually "hit" the head on the ball, with an attempt of 180 s and a throw of 80 balls	Addition of 1 and 2 mats respectively
3. Pinguim Slide	On WBB; performs laterolateral weight transfer in order to "catch" the largest number of fish, with 3 attempts of 60 s	Addition of 1 and 2 mats respectively
4. Ski Slalom	On WBB; performs laterolateral weight transfer for the purpose of deflecting obstacles, and anteroposterior weight transfers to control speed while skiing on the mountain, with three 60-s attempts	Addition of 1 and 2 mats respectively
5. Table Tilt	On WBB; performs small laterolateral and anteroposterior displacements as a simulation of an unstable board to place the balls inside holes, with 3 attempts of initial 30 s. You gain 20 s every 1 level you reach so that you do not exceed 180 s	Addition of 1 and 2 mats respectively
6. Free Steps	Up and down WBB, alternating feet with eyes open for 180 s	Addition of weights of 1 kg and 2 kg, respectively
7. Balance Bubble	On WBB; performs laterolateral and anteroposterior body displacement without the bubble touching the banks of the virtual river for 180 s	Addition of 1 and 2 mats respectively

Legend: Each game will be executed for 3 minutes with a rest interval of approximately 1 minute; *The mats (height: 3 x width: 43 x length: 93 cm) will be used to create an unstable surface.

The games were pre-established with a focus on balance and demands similar to that of the kinesiotherapy protocol: saccadic stimulation,

visuovestibular cephalic movement, proprioceptive stimulus, dynamic balance training, static gait, ankle and hip strategies, fine CoP control, stimulus optokinetic, double task (motor), and motor coordination[51-53]; and all scores obtained in games will be noted. The progressions will happen upon adaptation of the patient, recommending 2 evolutions, respectively, in the 6th and 13th sessions.

Adherence

Participants will be contacted by telephone to confirm assessment and training sessions to avoid sample loss. Replacement of faults and performed interventions by engaged and motivated professional will be performed to increase adherence. Regardless of the protocol, the criteria for non-adherence will be considered as follows: (1) absence > 30% of the intervention, consecutively and without replacement; (2) presenting persistent pain or severe discomfort (headache, vomiting, dizziness, etc.), which prevents continuity in performing the proposed protocol in future sessions (or both); (3) presenting hemodynamic instability: descompensation of systemic arterial pressure (systolic and diastolic values > 200 mmHg and 110 mmHg, respectively)[54] and HR above the submaximal values allowed during the training maintained even after pauses, calculated by means of the formula [HRsub = 0.75 × (220 − age)][55]; (3) those who do not adapt to the proposed intervention.

Data acquisition

For data collection of the CoP variables, 6 static balance tests will be performed on the FP based on their complexity variation and common use in

the literature[56,57]: bipodal support on a stable surface with eyes open and eyes closed for 30 s each; unipodal support of paretic limbs on a stable surface with eyes open and eyes closed for 30 s each; unipodal support of non-paretic limb on a stable surface with eyes open and eyes closed for 10 s each. The distance between the patients' feet will be standardized[51] and in unipodal support tasks, the contralateral knee may be slightly flexed and there may be no contact between the raised and support leg. Each test can have 1 successful attempt and a maximum of 3 unsuccessful attempts. The attempt is considered invalid if the participant moves their support leg or touches the floor with the contralateral leg[58].

For gait analysis during 6MTW, the camera will be positioned perpendicular to the plane of motion, at a height of 1 m and 3 m away from the subject to capture gait pattern of the hemiparetic side, and will be considered as complete gait cycle. Markers will be placed on the main bone references of the paretic lower limb (greater trochanter of the femur, lateral tibial condyle, lateral fibular malleolus, fifth metatarsal head, and lateral calcaneal bone tuberosity) for further analysis.

For encephalographic recording during the FP static balance and walking tests, the Emotiv Epoc headset will be positioned on the user's head according to the international placement in 10-20 positioning system following the manufacturer's specifications[59].

Data processing

The Bertec® Model 4060 platform will be synchronized with Qualisys Motion Capture Systems (Qualisys Medical AB, 411 13 Gothenburg, Sweden),

and through that system software, Qualisys Track Manager, data for CoP will be collected and converted to MATLAB compatible files (the Mathworks, Natick, RI, USA). The sampling rate will be 40 Hz, and a Butterworth bandpass filter with a cutoff frequency of 15 Hz will be applied to eliminate noise contamination.

For kinematic analysis, the videos will be converted to an Audio Video Interleave (AVI) file extension and exported to Kinovea software. Hip, knee, and dorsiflexion flexion angles will be evaluated in the middle oscillatory phase of gait, using as reference the follows joints: hip, tibiofemoral metatarsophalangeal and calcaneal. Emotiv EPOC data processing will follow the model used by Oliveira *et al.*[60] (2018). The encephalographic recording will take place during gait and static balance tests, using 10 s of single-leg support activity and a central 10-s cut-out in bipodal support activities.

Statistical analysis

The SPSS (Statistical Package Social Science) V.21.0 software program will be used and significance level of 5% and CI of 95% will be implemented for all statistical analyses. Descriptive analysis of the sample characterization variables will be performed through central tendency and dispersion measures.

The Kolmogorov-Smirnov test will initially be performed to evaluate the normality of the data. To intragroup comparisons t-Student test or Wilcoxon test will be used. Intergroup comparisons will be evaluated using ANOVA or Kruskal-Wallis, depending on the normality of the data. Intention-to-treat analysis will be performed for dropout data, considering the last data obtained from the participant.

Patient and public involvement

Patients were not involved in the design of this trial, establishing the research question or developing recruitment procedures. At the end of the study, the results will be reported to the participants in the form of a lecture, showing the effects found in the studied variables. The results of the study will be disseminated to participants through social networks and will be submitted to a peer-reviewed journal and scientific meetings.

Ethics and dissemination

This research was approved by the Research Ethics Committee of the Federal University of Rio Grande do Norte, with protocol number 3.434.350 in July 3, 2019 and trial registration number RBR-78v9hx (Brazilian Registry of Clinical Trials). Participants will be informed of the study objectives, its risks and benefits, and when eligible for inclusion, if they agree to participate, must sign the informed consent before the study begins. They will be free to abandon the study at any time without the obligation of giving any explanation.

There will be prior contact with individuals through social networks, when all information about the study will be presented, as well as the Resolution No. 466/2012 of the Brazilian National Health Council of 2012, which provides guidelines and standards for research involving human subjects. In case any negative effects occur, participants who suffer harm from trial participation will receive physical assistance according to the injury. The study results will be disseminated to participants through social networks and will be submitted to a peer-reviewed journal and scientific meetings.

Protocol amendments

Protocol amendments will be documented with a description of the change and the date of the change.

Study status

Subject recruitment is underway, started at November 2019, but the first inclusion was in January 2020. To date, eight patients were enrolled. The recruitment period spans over October 2020 with the goal to include 21 patients per treatment group, each patient completing the rehabilitation program and evaluation before, after and 8 weeks later.

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Authors' contributions

NPOSB led the study design and wrote the manuscript. BFLF, CSPM, TSR, TFC, FACC have made substantial contributions to the design of the study. NPOS, BFLF participate in the patient recruitment, and data collection. All the authors reviewed and approved the manuscript.

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Competing interests

None declared.

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Figure Legends

Figure 1. Schedule of enrollment, interventions, and assessments. Legend: t_1 1st week, t_{10} 10th week, t_{post10} post-training, t_{18} 18th week.

Figure 2. The schematic study design.

	STUDY PERIOD				
	Pre-treatment		Post-allocation	Post-treatment	
TIMEPOINT	$-t_1$	0	t_1 to t_{10}	t_{post10}	t_{18}
ENROLMENT:					
Eligibility screen	X				
Informed consent	X				
Allocation		X			
INTERVENTIONS:					
Control Group					
Experimental Group					
ASSESSMENTS:					
Postural balance deficits	X				
Cognitive screening	X				
Spasticity	X				
Ability to walk	X				
Stroke severity	X				
Clinical and demographic data		X			
Cardiovascular parameter variables		X	X	X	X
Adverse symptoms, perceived effort and pain			X		
Postural balance		X		X	X
Gait speed and kinematic analysis		X		X	X
Cortical Activation Patterns		X		X	X
Functional independence		X		X	X
Quality of life		X		X	X
Motivation				X	
Adverse events					X

Figure 1. Schedule of enrollment, interventions, and assessments. Legend: t1 1st week, t10 10th week, tpost10 post-training, t18 18th week.

170x224mm (300 x 300 DPI)

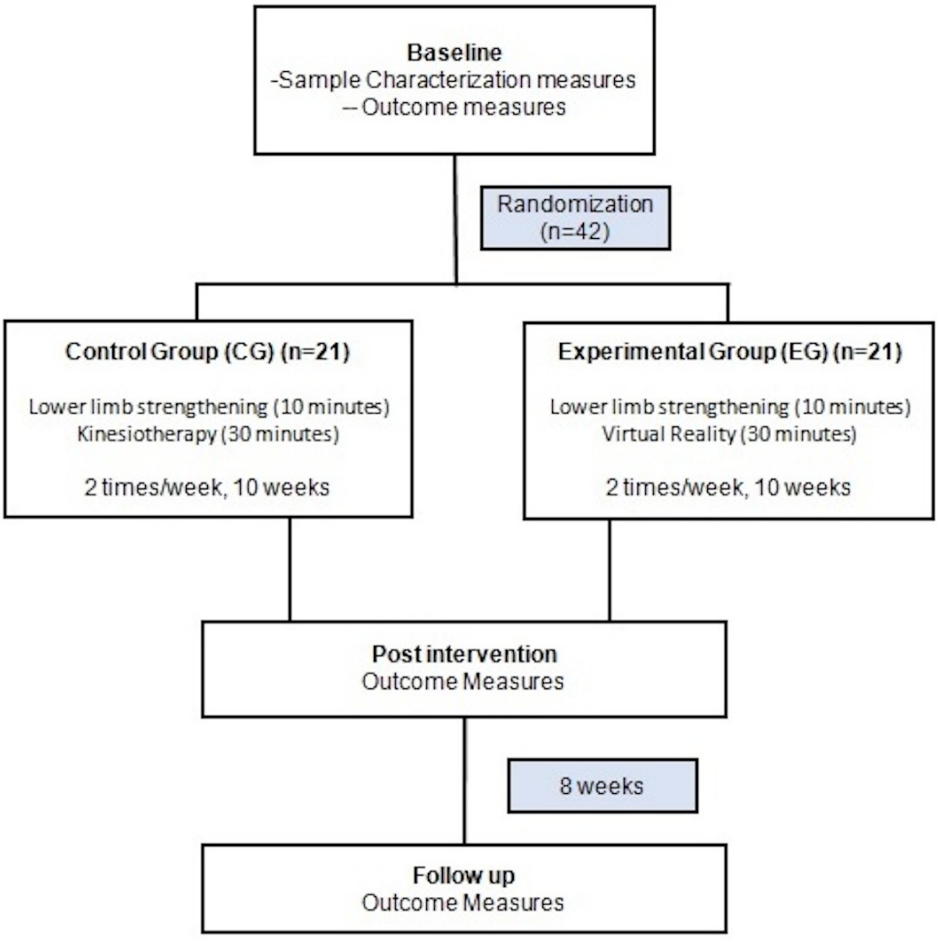

Figure 2. The schematic study design.

95x90mm (300 x 300 DPI)

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2; 210
	2b	All items from the World Health Organization Trial Registration Data Set	20
Protocol version	3	Date and version identifier	1
Funding	4	Sources and types of financial, material, and other support	21
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1; 21
	5b	Name and contact information for the trial sponsor	21
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	Not applicable
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	Not applicable
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-6

	6b	Explanation for choice of comparators	4-6
Objectives	7	Specific objectives or hypotheses	6
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	6; Figure 2
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6; 7
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	7
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	13-17; Table 1; Table 2; Table 3.
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	14
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	17
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	14
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	10-13; Figure 1
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figure 1
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	7; 8

Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	8
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	8
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	8
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	8
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	8
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	8
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	9-13
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	13; 17
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	8

Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	17-19
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	19
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	19
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	Not applicable
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	8
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	13
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	Not applicable
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	20
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	21
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	20
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	20

Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	20
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	21
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	20
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	20
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	20
	31b	Authorship eligibility guidelines and any intended use of professional writers	Not applicable
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	Not applicable
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Available if requested (not in protocol)
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	Not applicable

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

BMJ Open

Effects of exergames training on Postural Balance in chronic stroke patients: study protocol for a randomized controlled trial

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Effects of exergames training on Postural Balance in chronic stroke patients: study protocol for a randomized controlled trial

Nathalia Priscilla Oliveira Silva Bessa[1]; Bartolomeu Fagundes de Lima Filho[1]; Candice Simões Pimenta de Medeiros[1]; Tatiana Souza Ribeiro[1]; Tânia Fernandes Campos[1]; Fabrícia Azevedo da Costa Cavalcanti[1].

[1] Departament of Physical Therapy, Federal University of Rio Grande do Norte, Natal, Brazil.

*Corresponding author: Nathalia Priscilla Oliveira Silva Bessa. Laboratory of Virtual Reality, Departament of Physical Therapy, Federal University of Rio Grande do Norte, Senador Salgado Filho Av, 3000, Natal, Rio Grande do Norte, Brazil. Email: nathyzinhasilva@gmail.com

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Abstract

Introduction: Exergames training, as an additional therapy to standard care, has been widely used for motor recovery after stroke patients, and it is a valuable and positive tool in the rehabilitation of this population. This study describes a single-blind randomized clinical trial that will aim to investigate the effects of exergames training on postural balance in patients with chronic stroke.

Methods and analysis: Forty-two individuals with chronic stroke (> 6 months), aged 20 to 75 years, will be randomized into two groups: the experimental group, which will be subjected to an exergames protocol, and control group, which will undergo a kinesiotherapy protocol. Both protocols are based on postural balance. The intervention will consist of 40-minute sessions twice a week for 10 consecutive weeks. The volunteers will be evaluated before the treatment, at the end of the interventions, and 8 weeks thereafter. The primary outcome will be postural balance (Berg Balance Scale, Functional Reach Test, Timed Up and Go test, and Center of Pressure variables), and secondary outcomes will include gait (6-m timed walk and Kinovea Software), cortical activation patterns (EEG Emotiv EPOC), functional independence (Functional Independence Measure), quality of life (Stroke-Specific Quality of Life Scale), and motivation (Intrinsic Motivation Inventory).

Ethics and dissemination: This protocol was approved by the Ethics Committee of the Federal University of Rio Grande do Norte (number: 3.434.350). The results of the study will be disseminated to participants through social networks and will be submitted to a peer-reviewed journal and scientific meetings.

Trial registration number: RBR-78v9hx (Brazilian Registry of Clinical Trials – ReBEC).

Keywords: Stroke, Randomized Controlled Trial, Postural balance, Rehabilitation, Physical therapy modalities, Video Games.

Strengths and limitations of this study

- This study will explore objective data of postural balance and gait through the force platform and kinematic analysis.
- This study is among the few that use EEG to assess brain activity in stroke individuals undergoing an experimental protocol with exergames.
- The results of this research can lead to improvements in the use of exergames for postural balance in stroke rehabilitation.
- This study should benefit participants not only in physical aspects but also in psychological and social aspects.
- Blinding of participants will be not possible because of the nature of the intervention.

Introduction

According to the World Health Organization, cerebrovascular disease was the leading cause of death worldwide in 2016. Of those deaths, 5.78 million were directly attributed to stroke, making it the main non-communicable cause of death[1]. In Brazil, stroke resulted in approximately 100,000 deaths in 2014[2], and data indicate that approximately 568,000 affected individuals suffer from severe disability, making stroke the leading cause of disability in adults[3].

Following stroke, various aspects of balance function are altered, such as delay in regaining the ability to assume the standing posture, loss of balance, asymmetry between the right and left limbs, increased postural sway, and decreased weight bearing on the affected side[4,5]. Postural balance is important for functional tasks such as sitting, sit-to-stand, and walking. Dysfunction leads to alterations in weight distribution patterns, causing the paretic leg to take less load[6]. These changes increase the risk of falling, cause difficulties in executing functional activities, and cause reduction in performance of daily living activities, leading to a consequent reduction in social participation, which can aggravate the clinical situation[7].

Underuse of the impaired limb results in suppression of the cortical representation of the affected limb and further inhibition of its use[8]. The existence of cortical neural resources specialized in capturing changes in postural stability, which have been detected by changes in electroencephalography (EEG), supports the idea that postural adjustments are not only due to muscle responses to disorders but also due to cortically controlled intentional movements that may be altered following stroke[9].

One major component of stroke rehabilitation is exercise therapy,[10] and motor skill learning is particularly attractive because practice-induced improvement of sensorimotor performance supports the development of new aptitudes, providing the flexibility to adapt to changing conditions[11].

From this perspective, exergames training has been widely used in rehabilitation with the aim of improving sensorial, cognitive, psychological, and motor function[12,13]. They have been characterized as experiences that simulate a real environment in which the user can interact with the scenario created by the game through the involvement of multisensory aspects[14]. Exergames applications have the potential to apply relevant concepts of neuroplasticity, such as repetition, intensity, and task-oriented training of the paretic extremity[7], and may entrain several brain areas involved in motor planning and learning, thus leading to an enhanced motor performance in rehabilitation[12,15,16].

There are some evidences to suggest the effectiveness of exergames in improving upper limb function and balance as an additional therapy to standard care in stroke patients. Therefore, therapy based on exergames is a valuable and positive tool for the rehabilitation of this population[17,18].

A meta-analysis by Lee *et al.* (2019) found moderate evidence to support the effect of exergames training on improved lower limb function, including balance and gait, to a similar degree as upper limb function in chronic stroke patients, suggesting that this technique may be used as a complementary treatment method alongside traditional rehabilitation therapy. However, most of the studies in this meta-analysis increased the overall treatment time by adding exergames training to conventional treatment, which may be the reason for the observed outcomes[19].

Considering the above evidence, it is paramount to investigate the isolated effectiveness of exergames rehabilitation and its contributions to positive changes in postural balance in stroke patients, as this may provide additional evidence for the rehabilitation process in this population. From this perspective, it is hypothesized that training based on exergames improves postural balance, cortical activation, functionality, quality of life, and motivation of patients with chronic stroke.

The purpose of this study to investigate the effects of exergames training on postural balance in patients with chronic stroke and to explore changes in cortical activation patterns, functionality, quality of life, and motivation.

Methods and Analysis

Design

A single-blind randomized controlled clinical trial that follows the recommendations of the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)[20] will be carried out (Figure 1). . Participants will be randomized to receive the exergames protocol (experimental group, EG) and kinesiotherapy protocol (control group: CG) (Figure 2).

[INSERT Image 1]
[INSERT Image 2]

Participants

The study population will consist of forty-two chronic stroke patients who live in the city of Natal or nearby. A volunteer selection will be carried out at the stroke patient care centers in the city. The selection can also be carried out via spontaneous demand by the voluntary search of stroke patients after project

advertisement on social media. After this, the first telephone contact will be made to clarify any questions from the participants, and the first screening for inclusion will be performed.

Inclusion and exclusion criteria

The participants will be selected according to the following criteria: (1) first episode of unilateral stroke (ischemic or hemorrhagic); (2) postural balance deficits (Berg Balance Scale score -BBS) <45)[21]; (3) injury time ≥6 months; (4) age between 20 and 75 years; (5) at maximum level 2 of the modified Ashworth Scale to assess the spasticity of the paretic lower limb[22]; (6) good cognitive status based on the Mini-Mental State Examination (MMSE) (≥19 for illiterate, ≥24 for literate)[23]; (7) ability to walk without personal assistance indoors (Functional Ambulation Category -FAC) scores ≥3)[24]; (8) clinically stable, with no history of epilepsy or seizures in the last 6 months; (9) not having signs of unilateral neglect or sensory or global aphasia as assessed by National Institute Health Stroke Scale -NIHSS)[25]; (10) no uncorrected hearing and/or visual impairments; (11) not participating in a balance treatment protocol; and (12) ability to understand and obey simple motor commands.

Exclusion criteria will include (1) presenting other clinical conditions affecting balance and (2) pregnancy.

Sample Size

Using an online calculator[26] and based on previous study values (51.0±4.6 and 46.2±5.7)[27], a total sample of 42 participants (21 in EG and 21 in CG) will be sufficient to detect a clinically important difference between the

groups on the BBS. A statistical power of 80%, an alpha of 5% and a loss rate of 10% were considered for the sample calculation.

Randomization and blinding

A randomization sequence will be generated by a computer[28] in 3 blocks of 12 participants and 1 block of 6 participants, allowing participants to be equally distributed between the 2 groups. This stage will be conducted by a researcher who is not involved in the study, they will keep the randomization list confidential until the end of the study, and will organize the allocation in sequentially numbered opaque envelopes. These envelopes will be sealed, and the randomization sequence will be enforced using color coding for the study groups (blue and red), that will correspond to the protocol that will be executed. The contents of each envelope will be revealed at the beginning of each patient's training by the study therapists responsible for the intervention to maintain allocation confidentiality. The same therapists involved in CG training will perform training in the EG. The researcher responsible for evaluations will be blinded to all intervention groups. The only variables that will be collected during the training will be evaluated by the study therapists (non-blind). Statistical analysis will be performed by a blind researcher who will treat the groups according to color, and the equivalence between groups and colors will be revealed upon completion of the statistical analysis. The main researcher will have access to the final trial dataset; this researcher will decide on terminating the trial. All information about participants will be confidentiality before, during, and after the trial.

Evaluation procedures

The researchers will be trained before data collection procedures to ensure reliability of measurements, and the participants will be submitted to assessment using all the instruments mentioned below.

Measures

Sample characterization measures

- Cognition: The MMSE is a validated instrument in Brazil used to assess cognitive function. The total score ranges from 0 to 30 points, and the higher the score, the better the cognitive ability. Values are interpreted according to educational status. Good cognitive status is considered with scores of 24 points of higher for literate persons and 19 or higher for illiterate persons[23].
- Ability to walk: This will be evaluated by the FAC, which is a sensitive and reliable instrument for gait evaluation in stroke patients with hemiparesis[24] and ranks the ability to walk according to the amount of physical support required for the task. The score can vary from 0 (unable to walk or needs the help of 2 therapists) to 5 (independent in locomotion).
- Spasticity: The modified Ashworth scale allows the subjective assessment of muscle tone and classifies the affected segments from 0 (normal tone) to 5 (rigid affected part)[22].
- Clinical and demographic data: Personal, anthropometric, demographic, and pathological data (including, injury time, paretic side, stroke type),

and clinical history (history of falls, physical therapy treatment, and previous use of exergames) will be collected.

- Neurological impairment: NIHSS is a specific instrument to assess the severity of stroke via 10 items, and has been reported to have excellent validity and reliability[25].

Outcome measures

All outcome measures will be assessed in both intervention groups. The primary outcome measures considered in this study are as follows:

Postural Balance:

- Berg Balance Scale: BBS is a valid and reliable instrument for measuring both the static and dynamic aspects of balance in people after stroke. BBS scores range from 0 to 56, and values below 45 points are predictive of falls, indicating a significant change in balance[21,29]. In the present study, test scores with the paretic limb positioned behind will be used in item 13 and unipodal support over the paretic limb will be used in item 14, minimizing the ceiling effect in individuals with better balance[30].
- Functional Reach Test (FRT): FRT assesses a patient's stability by measuring the maximum forward distance an individual can reach while standing in a fixed position. It is widely used to identify the risk of falling[31]. Displacements < 15 cm indicate patient fragility and risk of falls[32].
- Timed up and Go (TUG) test: It is a valid instrument for assessing mobility and functional balance involving power, speed, and agility[33]. Performing the test within 10 seconds is considered normal for healthy,

independent adults without the risk of falls. Values from 11 to 20 seconds are expected for disabled or frail elderly people with partial independence and a low risk of falls. Values > 20 seconds suggest significant physical mobility deficits and risk of falls[34].

Center of Pressure (CoP) variables: Data for total displacement, anteroposterior, and midlateral velocity of the CoP will be assessed using the gold standard equipment for balance assessment, the force platform (FP)[35]. The Bertec® model 4060 connected to an external amplifier (Bertec® AM651X) will be used.

The secondary outcome measures considered in this study are as follows:

Cortical Activation Pattern

Alpha and beta waves will be evaluated based on their relationship with the motor learning process[36], using the Emotiv EPOC® portable 14 sensor electroencephalography (EEG) device, a gyroscope capable of detecting changes in the movement performed.

Gait kinematic analysis

The spatiotemporal and angular gait variables will be evaluated using the 6-m timed walk test and Kinovea® software.

- Six-meter timed walk (6MTW): It is a valid and reliable test for the assessment of the walking ability of patients with stroke[37]. Gait speed should be self-selected and considered comfortable and usual for the

participant. Studies show variation in mean habitual speed (0.45 m/s - 0.78 m/s) of gait in individuals with hemiparesis[38,39].

- Software Kinovea®*:* Kinematic evaluation will be performed during gait video capture (6MTW) using the Sony DCR-DVD850 digital cam, 2.7/6.7 cm LCD screen, and 60x optical zoom. Data will later be exported to Kinovea® 0.8.15 software for paretic lower limb angle and gait speed analysis. This is a public domain video editing and analysis software that is valid, reliable, and capable of accurately measuring distances up to 5 m from the object[40].

Functional independence

The Functional Independence Measure (FIM) scale is used because of its reliability, validity, precision, and feasibility criteria. It is composed of 18 items, including motor and cognitive items. Here the patient's answers are valued from 1 (total dependent) to 7 (complete independence), and the total punctuation ranges between 18 and 126. For this research, the FIM will be applied exclusively to the motor items, limiting the minimum score to 13 and the maximum to 91 points[41].

Quality of life

Quality of life perception will be assessed through a quality-of-life assessment scale for stroke (Stroke-Specific Quality of Life Scale [SS-QoL]). It is valid and reliable in assessing the quality of life after stroke in the Brazilian population and has 49 items distributed over 12 domains[42].

Motivation

The intrinsic motivation inventory (IMI) is a multidimensional measurement with 6 subscales used to assess the subjective experiences of participants when developing an activity and attends to the reliability and validity criteria. According to the inventory, instruction participants ranked their agreement with each statement on a Likert scale of 1 ("not at all true") to 7 ("very true")[43].

Participant monitoring measures

Participants will be monitored during interventions using the following measures:

- Cardiovascular parameter variables: Heart rate (HR) will be checked using a portable oximeter and blood pressure (BP) using a sphygmomanometer (Visomat Comfort III®, Incoterm, São Paulo, Brazil) on the non-paretic arm.
- Adverse symptoms, perceived effort, and pain: Information regarding headache, vomiting, and dizziness will be collected. Quantification of perceived effort and pain will be used as indicators to monitor exercise tolerance through the CR-10 (Category-Ratio Scale) Borg Scale[44] modified by Foster *et al*. [45] (2001).

Adverse events

Additional information such as hospitalizations, falls, out-of-routine medical consultation, medication change, new diagnosis, and presence of adverse events will be collected during the follow-up.

Interventions

The protocols in both groups will be performed individually through 40-minute sessions twice a week for 10 weeks (total of 20 sessions), totaling 13 hours of intervention[12,17,46]. The same outcome measures and motivation will be collected again at the end of the interventions (post-training) and after 8 weeks of the end of the interventions (follow-up). All participants will be instructed not to perform any other physical activity that works on body balance during the study period.

During each session, absences, manifestations of adverse symptoms, and occurrence of imbalance and/or falls will be recorded. Interventional modifications will be performed according to the patient's level of adaptation involving optimization of time or number of repetitions, and/or rest time enlargement, and all will be registered.

Both groups will begin their protocols with adapted lower limb strength training for 10 minutes[47,48] as described in Table 1. Each exercise should be performed with respect to the patient's level of adaptation and evolution will occur in the 6th and 13th sessions using the materials described.

Table 1. Lower limb strengthening exercises.

Exercise	Evolution	Materials Used	Sets
1. Get up and sit on a chair	Surface change	1 or 2 mats to create an unstable surface (H: 3 x W: 43 x L: 93 cm).	2 sets of 60 seconds with 30 seconds of rest
2. Go up and down steps	Increase the step height; add weight	Larger step and 1 kg shin pad.	
3. Strengthening of hip extensors	Add weight	1 kg and 2 kg shin pad.	

4. Tiptoe rise	Add weight	1 kg and 2 kg shin pad.

Source: Adapted from Allet et al. (2010).

Control Group

Participants in the CG will receive a kinesiotherapy protocol (30 minutes) (Table 2), focusing on balance based on previous studies, and that promotes stimuli similar to the EG, selected so they demand identical motor sensors in both intervention environments, real and virtual[47-50]. Two progressions will happen, in the 6th and 13th sessions.

Table 2. Kinesiotherapeutic protocol exercises.

Exercise	Evolution	Materials Used	Sets**
1. Gait training on a stable surface.	Gait training on an unstable surface using mats; addition of shin pads of 1 kg.	Mat* and 1 kg shin pads.	2 sets of 3 minutes
2. Laterolateral weight transfer and discharge.	Addition of 1 and 2 mats respectively.	Mat	3 sets of 60 seconds
3. Anteroposterior weight transfer and discharge.	Addition of 1 and 2 mats respectively.	Mat	3 sets of 60 seconds
4. Laterolateral cephalic movement with eyes open.	Same movement with eyes closed. Added an exercise mat.	Mat	3 sets of 60 seconds
5. Anteroposterior cephalic movement with eyes open.	Same movement with eyes closed. Added an exercise mat.	Mat	3 sets of 60 seconds
6. Dissociation of scapular and pelvic girdles.	Addition of 1 and 2 mats respectively.	Mat	3 sets of 2 minutes

Source: Adapted from Nascimento, Patrizzi, Oliveira (2012); Soares, Sachelli (2008); Allet et al. (2010) e Ribeiro (2015). Legend: *The mats (height: 3 x width: 43 x length: 93 cm) will be used to create an unstable surface; **For each series performed, the participant will be entitled to 30 seconds of rest.

Experimental Group

Participants in the EG will receive seven Wii Fit Plus exergames on the Nintendo Wii® (30 minutes) (Table 3). This will use the Wii Balance Board (WBB) accessory, a multimedia projector, and the Wii Remote Controller. Initially, participants will have a moment to adapt to Nintendo Wii and its components. It is expected that the participants in this group will be able to deal satisfactorily with the games used in the protocol after adaptation. Otherwise, they will enter the non-adherence criteria.

Table 3. Exergames protocol exercises.

Game	Description	Progression
1. Free Run	Control in patient's pocket "marching" on firm surface	Addition of 1 and 2 mats* respectively
2. Soccer Heading	On WBB; performs anteroposterior and laterolateral weight transfer to virtually "hit" the head on the ball, with an attempt of 180 s and a throw of 80 balls	Addition of 1 and 2 mats respectively
3. Pinguim Slide	On WBB; performs laterolateral weight transfer in order to "catch" the largest number of fish, with 3 attempts of 60 s	Addition of 1 and 2 mats respectively
4. Ski Slalom	On WBB; performs laterolateral weight transfer for the purpose of deflecting obstacles, and anteroposterior weight transfers to control speed while skiing on the mountain, with three 60-s attempts	Addition of 1 and 2 mats respectively
5. Table Tilt	On WBB; performs small laterolateral and anteroposterior displacements as a simulation of an unstable board to place the balls inside holes, with 3 attempts of initial 30 s. You gain 20 s every 1 level you reach so that you do not exceed 180 s	Addition of 1 and 2 mats respectively
6. Free Steps	Up and down WBB, alternating feet with eyes open for 180 s	Addition of weights of 1 kg and 2 kg, respectively

7. Balance Bubble	On WBB; performs laterolateral and anteroposterior body displacement without the bubble touching the banks of the virtual river for 180 s	Addition of 1 and 2 mats respectively

Legend: Each game will be executed for 3 minutes with a rest interval of approximately 1 minute; *The mats (height: 3 × width: 43 × length: 93 cm) will be used to create an unstable surface.

The games were pre-established with focus on balance, and demands similar to that of the kinesiotherapy protocol: saccadic stimulation, visuovestibular cephalic movement, proprioceptive stimulus, dynamic balance training, static gait, ankle and hip strategies, fine CoP control, stimulus optokinetic, double task (motor), and motor coordination[51-53]. All scores obtained in games will be noted. Progression will occur upon adaptation of the patient, 2 evolutions will occur, in the 6th and 13th sessions.

Adherence

Participants will be contacted by telephone to confirm assessment and training sessions to avoid sample loss. Strategies to improve adherence include making up for missed sessions and interventions of motivated professionals. Regardless of the protocol, the criteria for non-adherence will be considered as follows: (1) absence > 30% of the intervention, consecutively and without make-up sessions; (2) presenting persistent pain or severe discomfort (headache, vomiting, dizziness, etc.), which prevents continuity in performing the proposed protocol in future sessions (or both); (3) presenting hemodynamic instability: decompensation of systemic arterial pressure (systolic and diastolic values > 200 mmHg and 110 mmHg, respectively)[54] and HR above the submaximal values allowed during the training maintained even after pauses, calculated by

means of the formula [HRsub = 0.75 × (220 − age)][55]; and (3) those who did not adapt to the proposed intervention.

Data acquisition

For data collection of the CoP variables, 6 static balance tests will be performed on the FP based on their complexity variation and common use in the literature[56,57]: bipodal support on a stable surface with eyes open and eyes closed for 30 s each; unipodal support of paretic limbs on a stable surface with eyes open and eyes closed for 30 s each; unipodal support of non-paretic limb on a stable surface with eyes open and eyes closed for 10 s each. The distance between the patients' feet will be standardized[51] and in unipodal support tasks, the contralateral knee may be slightly flexed, and there may be no contact between the raised and support legs. Each test can have 1 successful attempt and a maximum of 3 unsuccessful attempts. The attempt is considered invalid if the participant moves their support leg or touches the floor with the contralateral leg[58].

For gait analysis during 6MTW, the camera will be positioned perpendicular to the plane of motion, at a height of 1 m and 3 m away from the subject to capture the gait pattern of the hemiparetic side, and will be considered as a complete gait cycle. Markers will be placed on the main bone references of the paretic lower limb (greater trochanter of the femur, lateral tibial condyle, lateral fibular malleolus, fifth metatarsal head, and lateral calcaneal bone tuberosity) for further analysis.

For encephalographic recording during the FP static balance and walking tests, the Emotiv Epoc headset will be positioned on the user's head according

to the international placement in the 10-20 positioning system following the manufacturer's specifications[59].

Data processing

The Bertec® Model 4060 platform will be synchronized with Qualisys Motion Capture Systems (Qualisys Medical AB, 411 13 Gothenburg, Sweden), and through that system software, Qualisys Track Manager, data for CoP will be collected and converted to MATLAB compatible files (Mathworks, Natick, RI, USA). The sampling rate will be 40 Hz, and a Butterworth bandpass filter with a cutoff frequency of 15 Hz will be applied to eliminate noise contamination.

For kinematic analysis, the videos will be converted to an Audio Video Interleave (AVI) file extension and exported to Kinovea software. The hip, knee, and dorsiflexion flexion angles will be evaluated in the middle oscillatory phase of gait, using the following joints: hip, tibiofemoral metatarsophalangeal, and calcaneal. Emotiv EPOC data processing will follow the model used by Oliveira *et al.*[60] (2018). The encephalographic recording will take place during gait and static balance tests, using 10 s of single-leg support activity and a central 10-s cutout in bipodal support activities.

Statistical analysis

The SPSS (Statistical Package Social Science) V.21.0 software program will be used, and a significance level of 5% and CI of 95% will be implemented for all statistical analyses. A descriptive analysis of the sample characterization variables will be performed through central tendency and dispersion measures.

Normality tests (Kolmogorov-Smirnov) will be used for outcomes and will be compared between groups within each training session by using intergroup comparisons, t tests for independent samples, or Mann–Whitney U tests. A mixed analysis of variance (ANOVA) with repeated measures will be used to compare values and variations of outcome measures, comparing values between groups and between baseline, post-training, and follow-up assessments.

The effect size will be calculated using GPower 3.1.9.3 (University of Dusseldorf, Kiel, Germany). Cohen's d will be used to calculate the effect size between the control and the experimental groups, and the partial eta squared for intragroup analyzes[61]. Intention-to-treat analysis will be performed for dropout data, considering the last data obtained from the participant.

Risk of Bias and Study Limitation

The present study has a low risk of selection bias due to randomization and concealment of the allocation of participants; low risk of detection bias as the outcome assessor will be blind; high risk of performance bias because the participants will not be blind to the proposed therapies; reporting and attrition biases do not apply because it is a protocol study[62].

The proposed follow-up time (8 weeks) can be considered a potential (minor) study limitation; it is not verified whether motor and neurophysiological changes resulting from the proposed intervention will be maintained over a long term (1 year). However, it is suggested that the effect of treatment with Nintendo Wii can be maintained for at least 2 months after the intervention, with improvements in motor recovery.

Patient and public involvement

Patients were not involved in the design of this trial, establishing the research question, or developing recruitment procedures. At the end of the study, the results will be reported to the participants in form of a lecture, showing the effects found in the studied variables. The results of the study will be disseminated to participants through social networks and will be submitted to a peer-reviewed journal and scientific meetings.

Ethics and dissemination

This research was approved by the Research Ethics Committee of the Federal University of Rio Grande do Norte, with protocol number 3.434.350 on July 3, 2019 and trial registration number RBR-78v9hx (Brazilian Registry of Clinical Trials). Participants will be informed of the study objectives, its risks and benefits, and when eligible for inclusion, if they agree to participate, must sign the informed consent before the study begins. They will be free to abandon the study at any time without the obligation to give any explanation.

There will be prior contact with individuals through social networks, when all information about the study will be presented as well as the Resolution No. 466/2012 of the Brazilian National Health Council of 2012, which provides guidelines and standards for research involving human participants. In case any negative effects occur, participants who suffer harm from trial participation will receive physical assistance according to the injury. The study results will be disseminated to participants through social networks and will be submitted to peer-reviewed journals and scientific meetings.

Protocol amendments

Protocol amendments will be documented with descriptions of the change and the date of the change.

Study status

Subject recruitment is underway, started in November 2019, but the first inclusion was in January 2020. To date, eight patients were enrolled in the study. The recruitment period spans till January 2021. The goal is to include 21 patients per treatment group, each patient completing the rehabilitation program and evaluation before and after, and 8 weeks later.

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Authors' contributions

NPOSB led the study design and wrote the manuscript. BFLF, CSPM, TSR, TFC, and FACC have made substantial contributions to the design of the study. NPOSB and BFLF participate in participants' recruitment and data collection. All authors reviewed and approved the manuscript.

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Competing interests

None declared.

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Figure Legends

Figure 1. Schedule of enrollment, interventions, and assessments. Legend: t_1 1st week, t_{10} 10th week, t_{post10} post-training, t_{18} 18th week.

Figure 2. The schematic study design.

	STUDY PERIOD				
	Pre-treatment		Post-allocation	Post-treatment	
TIMEPOINT	$-t_1$	0	t_1 to t_{10}	t_{post10}	t_{18}
ENROLMENT:					
Eligibility screen	X				
Informed consent	X				
Allocation		X			
INTERVENTIONS:					
Control Group					
Experimental Group					
ASSESSMENTS:					
Postural balance deficits	X				
Cognitive screening	X				
Spasticity	X				
Ability to walk	X				
Stroke severity	X				
Clinical and demographic data		X			
Cardiovascular parameter variables		X	X	X	X
Adverse symptoms, perceived effort and pain			X		
Postural balance		X		X	X
Gait speed and kinematic analysis		X		X	X
Cortical Activation Patterns		X		X	X
Functional independence		X		X	X
Quality of life		X		X	X
Motivation				X	
Adverse events					X

Figure 1. Schedule of enrollment, interventions, and assessments. Legend: t1 1st week, t10 10th week, tpost10 post-training, t18 18th week.

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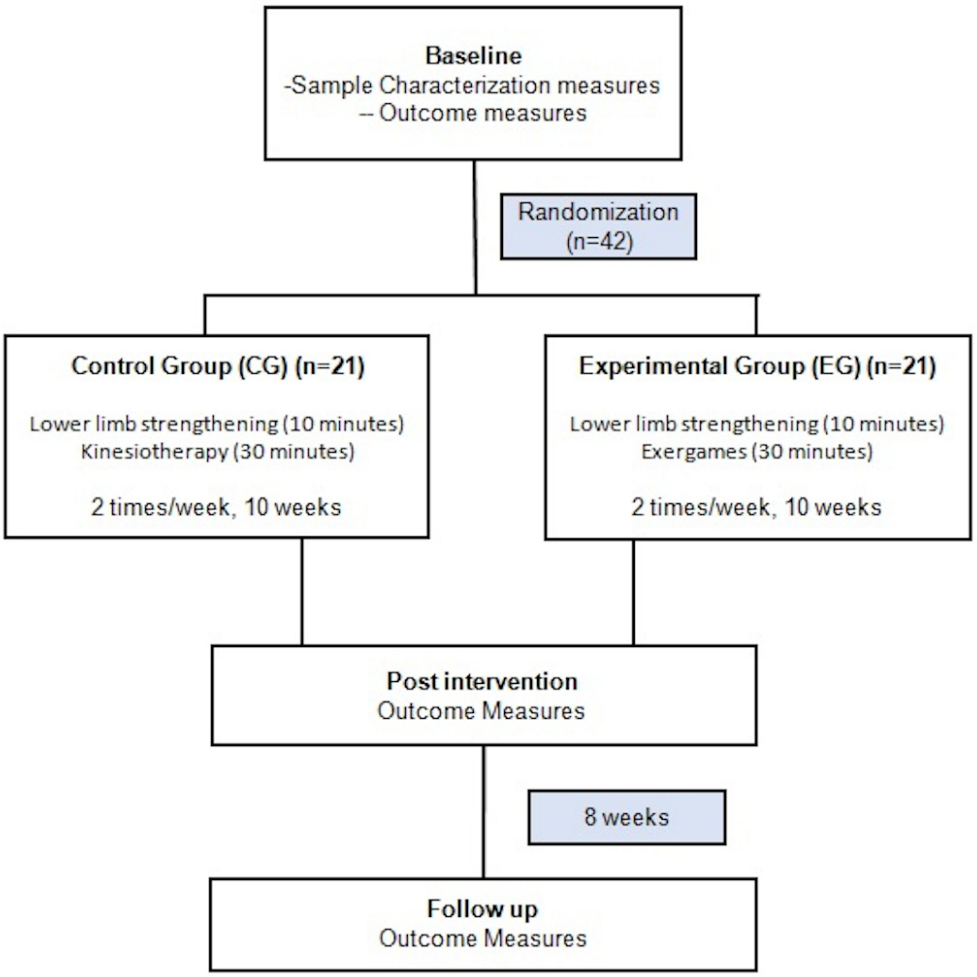

Figure 2. The schematic study design.

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SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2; 210
	2b	All items from the World Health Organization Trial Registration Data Set	20
Protocol version	3	Date and version identifier	1
Funding	4	Sources and types of financial, material, and other support	21
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1; 21
	5b	Name and contact information for the trial sponsor	21
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	Not applicable
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	Not applicable
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-6

	6b	Explanation for choice of comparators	4-6
Objectives	7	Specific objectives or hypotheses	6
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	6; Figure 2
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6; 7
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	7
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	13-17; Table 1; Table 2; Table 3.
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	14
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	17
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	14
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	10-13; Figure 1
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figure 1
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	7; 8

Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	8
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	8
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	8
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	8
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	8
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	8
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	9-13
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	13; 17
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	8

Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	17-19
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	19
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	19
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	Not applicable
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	8
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	13
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	Not applicable
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	20
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	21
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	20
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	20

Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	20
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	21
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	20
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	20
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	20
	31b	Authorship eligibility guidelines and any intended use of professional writers	Not applicable
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	Not applicable
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Available if requested (not in protocol)
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	Not applicable

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.