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Effect of tDCS combined with virtual reality for post-stroke cognitive impairment: a randomized controlled trial study protocol

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Abstract

Background Post-stroke cognitive impairment (PSCI) not only increases patient mortality and disability, but also adversely affects motor function and the ability to perform routine daily activities. Current therapeutic approaches for, PSCI lack specificity, primarily relying on and medication and traditional cognitive therapy supplemented by a limited array of tools. Both transcranial direct current stimulation (tDCS) and virtual reality (VR) training have demonstrated efficacy in improving cognitive performance among PSCI patients. Previous findings across various conditions suggest that implementing a therapeutic protocol combining tDCS and VR (tDCS - VR) may yield superior in isolation. Despite this, to our knowledge, no clinical investigation combining tDCS and VR for PSCI rehabilitation has been conducted. Thus, the purpose of this study is to explore the effects of tDCS - VR on PSCI rehabilitation.

Methods This 4-week, single-center randomized clinical trial protocol will recruit 200 patients who were randomly assigned to one of four groups: Group A (tDCS + VR), Group B (tDCS + sham VR), Group C (sham tDCS + VR), Group D (sham tDCS + sham VR). All four groups will receive conventional cognitive rehabilitation training. The primary outcome measurement utilizes the Mini-Mental State Examination (MMSE). Secondary outcome measures include the Montreal Cognitive Assessment, Frontal Assessment Battery, Clock Drawing Test, Digital Span Test, Logic Memory Test, and Modified Barthel Index. Additionally, S-YYZ-01 apparatus for diagnosis and treating language disorders assesses subjects' speech function. Pre- and post-four-week intervention assessments are conducted for all outcome measures. Functional near-infrared spectroscopy (fNIRS) is employed to observe changes in oxygenated hemoglobin (HbO), deoxy-hemoglobin (HbR), and total hemoglobin (HbT) in the cerebral cortex.

Discussion Our hypothesis posits that the tDCS - VR therapy, in opposed to individual tDCS or VR interventions, could enhance cognitive function, speech ability and daily living skills in PSCI patients while concurrently augmenting frontal cortical activity. This randomized study aims to provide a robust theoretical foundation supported by scientific

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evidence for the practical implementation of the tDCS - VR combination as a secure and efficient PSCI rehabilitation approach.

Trial registration Chictr.org.cn Identifier: ChiCTR2300070580. Registered on 17th April 2023.

Keywords Post-stroke cognitive impairment, Transcranial direct current stimulation, Virtual reality, Randomized controlled trial, Treatment

Introduction

Post-stroke cognitive impairment (PSCI) manifests as executive function, memory, computation, visuospatial ability, and language skills impairments in individuals following as stroke [1]. Beyond its association with increased mortality and disability [2], PSCI exerts detrimental effects on motor function and the ability to perform daily tasks, significantly impacting the predicted quality of life for stroke patients [3, 4]. The current PSCI rehabilitation program is marked by inadequate instruments and a reliance on medication and traditional cognitive therapy, lacking specificity. This approach often results in variable cognitive improvements, with different medications and poses challenges related to drug tolerance. Additionally, conventional cognitive rehabilitation tends to lead to reduced patient enthusiasm and poor compliance [5, 6]. Consequently, there is an urgent need for a safe, reliable, and effective treatment modality for PSCI rehabilitation.

Transcranial direct current stimulation (tDCS) emerges as a non-invasive brain stimulation approach that modulates transmembrane potential through the delivery of a weak constant current from the anode to the cathode, thereby enhancing or inhibiting cortical activity [7, 8]. Previous research substantiates the safety and efficacy of tDCS in PSCI, demonstrating improvements in working memory, concentration, unilateral neglect, and activities of daily living, without evidence of increased risk for adverse stroke events [9–11]. The stationary position of the electrode blades relative to the skull ensures treatment efficacy, even with patient movement. Moreover, the tDCS apparatus, readily available in numerous rehabilitation centers, is characterized by safety, practicality, and affordability. Consequently, tDCS presents itself as a superior and more effective approach to treating PSCI.

Virtual reality (VR) has been applied to improve cognitive impairment in patients [12]. VR, a non-invasive and pharmacological treatment approach, constructs a lifelike virtual environment incorporating tactile, visual, auditory, and kinesthetic elements. This is achieved through advanced technology, predominantly centered around a computer. The technology provides diverse feedback mechanisms, enabling patients to interact with objects in a virtual environment using various sensory stimuli, thereby transforming the potentially tedious rehabilitation training into a more engaging and straightforward process [13, 14]. Numerous studies affirm that VR significantly enhances memory, concentration, and problem-solving skills in patients following brain tumor surgery, older patients with mild cognitive impairment, as well as those with Alzheimer's disease, Parkinson's disease, and post-stroke convalescence [15–17]. Moreover, existing research suggests that early VR training post brain injury, especially after a stroke, substantially improves patients' overall cognitive function and specific cognitive modules such as executive function, memory, and attention [18, 19].

In individuals with post-stroke cognitive impairment, both tDCS and VR contribute to enhancing cognitive abilities. However, the findings indicate that combining tDCS and VR may yield superior results compared to each interventional alone [20–22]. VR technology, through peripheral-to-central stimulation enhances the enjoyment of therapy, motivation patients and fostering subjective initiative [23]. Meanwhile, transcranial direct current stimulation can facilitate the reorganization and recovery of the central nervous system by improving blood circulation in the brain and regulating the excitability of the cerebral cortex via central-to-peripheral stimulation [24, 25]. For instance, after undergoing 15 sessions involving cathodal tDCS to the overactive motor cortex, VR arm movement training, or a combination of both over three weeks, participants with upper extremity dysfunction following subacute stroke demonstrated significantly improved fine motor performance compares to the tDCS and VR only group [26]. Additionally, a study found that anodal tDCS administered to the ipsilateral M1 during VR training improves stroke patients' executive, cognitive, and upper limb function. While these studies offer foundational support for combination of tDCS and VR in stroke treatments, as of our knowledge cutoff, no clinical trial has been conducted to investigate this combination in post-stroke cognitive impairment patients.

Based on conventional cognitive rehabilitation, this study integrates tDCS and VR in patients with PSCI to leverage their respective advantages. This includes combining active and passive training and implementing a cycle of peripheral and central stimulation to generate synergistic effects, there by expediting the recovery of cognitive function. The study assesses the cognitive function, speech capabilities, and daily living ability to analyze

changes in various indicators before and after tDCS - VR treatment for cognitive impairment post stroke [22]. Additionally, functional near-infrared spectroscopy (fNIRS) is utilized before and after the intervention to observe changes in oxygenated hemoglobin (Oxy-Hb) and deoxyhemoglobin (Deoxy-Hb) levels in the frontal region [27].

We believe that the combination of tDCS and VR will more effectively enhance cognitive function, speech ability, and daily living capabilities in PSCI patients compared to individual interventions. Furthermore, we anticipate increased cortical activity from the frontal to temporal regions compared to using tDCS or VR alone. This randomized study aims to establish a robust theoretical foundation for the clinical application of tDCS – VR, offering a safe and effective strategy for PSCI rehabilitation.

Methods

Study design

This is a prospective, randomized, single-center study (Registration number: ChiCTR2300070580) conducted in the Department of Rehabilitation Medicine at The First Affiliated Hospital of Fujian Medical University, China. Approval has been obtained from the Ethics Committee of the First Affiliated Hospital of Fujian Medical University (Approval No.: MRCTA, ECFAH of FMU [2021]217). Hospitalized post-stroke cognitive impairment patients are invited to participate and are randomly assigned to Group A, Group B, Group C or Group D in a 1:1:1:1 ratio. Relevant assessments are conducted on the day of enrollment (T0) and after intervention (T1) to evaluate treatment effectiveness (Fig. 1; Table 1). The protocol adheres to the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guidelines [28, 29].

Participants

Recruitment

Recruitment is facilitated through posters in the inpatient and outpatient departments of The First Affiliated Hospital of Fujian Medical University. interested patients can contact the investigators by phone or WeChat.

Inclusion criteria

Patients eligible for the study must meet the following criteria:

1) The fourth National Cerebrovascular Disease Academic Conference of the Chinese Medical Association affirmed the diagnosis of ischemia or hemorrhage, which was supported by computed tomography (CT) or magnetic resonance imaging (MRI), and the diagnostic of stroke concurred with that diagnosis;
2) Patients aged 18–70 years within 6 months of stroke onset;
3) Meeting the diagnostic criteria of expert Consensus on the Management of PSCI (2021);
4) MMSE score: $10 < \text{MMSE} < 26$;
5) Able to cooperate with all assessments and voluntarily sign the informed consent.

Exclusion criteria

Patients meeting any of the following criteria will be excluded:

1) Severe illness or unconsciousness;
2) Metal implants in the head or artificial pacemaker;
3) Having a history of epilepsy or seizures;
4) Previous history of mental illness, severe aphasia or severe hearing or visual impairment;
5) Complicated with myocardial infarction, severe liver and kidney dysfunction, severe infection, or severe diabetes.

Sample size

The sample size, determined based on the pilot trial, focuses on the change in Mini-Mental State Examination (MMSE) scores after 4 weeks of tDCS and/or VR treatment. GPower v.3.1.9.7 calculated a minimum sample size of 180 (45 per group) with an effect size of 0.25, power of 0.8, and alpha of 0.05. Anticipating a 10% dropout rate, a conservative sample size of 200 participants (50 per group) as established.

Randomization and blinding

The statistician used SPSS 26.0 software to generate a numerical randomization scheme. The concealment of allocation will be performed using sealed envelopes with numbers and completed by the lead investigator. After completing the baseline assessment, the subjects will be randomly assigned to the corresponding group according to the sequence of enrollment in the study. Participants were given a 4-week intervention and assessed after the experiment was hosted. The entire process will strictly follow the uniform standards of the reporting test guidelines. Assessors will be blinded to group allocation. If an assessor becomes unblinded, this will be documented and reported.

Interventions

The 200 subjects in four groups will receive all conventional cognitive rehabilitation, including attention training, scratching exercises, deletion operation, problem solving ability training, calculation training, item

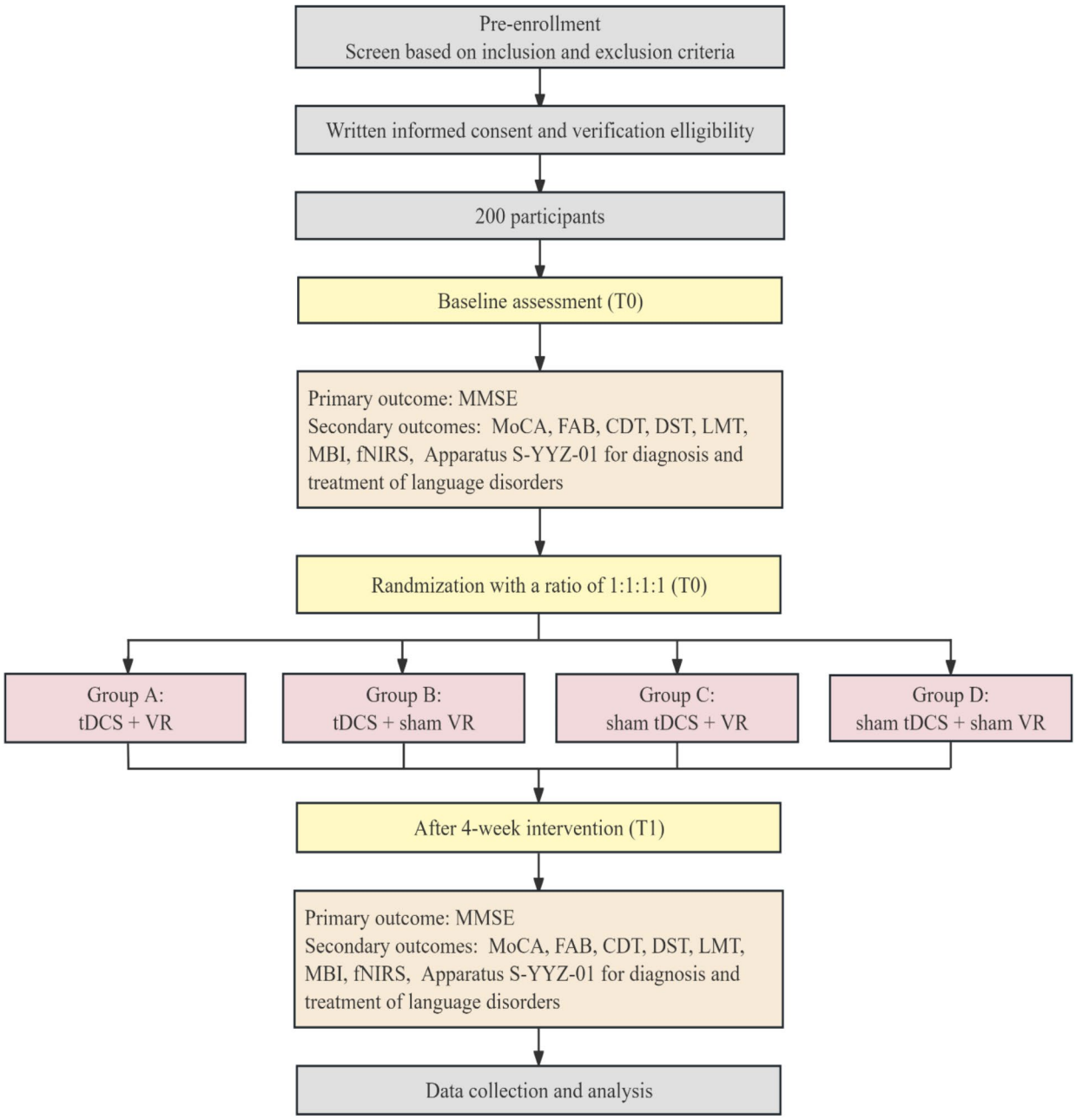

Fig. 1 Flow chart of study procedure. MMSE, Mini-Mental State Examination; MOCA, Montreal Cognitive Assessment; FAB, Frontal Assessment Battery; CDT, Clock Drawing Test; DST, Digital Span Test; LMT, Logic Memory Test; MBI, Modified Barthel Index; fNIRS, functional Near-infrared Spectroscopy; tDCS, transcranial Direct Current Stimulation; VR, virtual reality

classification, sequencing training. The treatment is carried out in four weeks, five times a week, 20 min each time.

Group A: tDCS + VR

Participants will undergo the combination of transcranial Direct Current Stimulation (IS300, SiChuan ZhiNeng Electronics Industrial Co., Ltd., China) and virtual reality (NEVRS301, BeiJing Noitom Technology Ltd., China). To ensure good electrical conductivity, they are immersed in 0.9% NaCl soaked surface sponge electrodes ($5cm^2$) on a current stimulator. The anode was posited on the left dorsolateral prefrontal cortex (DLPFC), while the cathode is placed on the opposite shoulder. We administer an intensity of 1.5 mA, gradually increasing the currented to 1.5 mA within the initial 30 s, eliciting a slight itchy

Table 1 Time schedule of enrollment and assessments

Study period visits	Pre-enrollment	T0	T1
Relative start of treatment days	−1 week	Day 0	±5 days after intervention
Eligibility screen	×		
Informed consent	×		
Demographics and medical data	×		
Allocation		×	
MMSE		×	×
MOCA		×	×
FAB		×	×
CDT		×	×
DST		×	×
LMT		×	×
MBI		×	×
fNIRS		×	×
Apparatus S-YYZ-01 for diagnosis and treatment of language disorders		×	×

Abbreviations: MMSE, Mini-Mental State Examination; MOCA, Montreal Cognitive Assessment; FAB, Frontal Assessment Battery; CDT, Clock Drawing Test; DST, Digital Span Test; LMT, Logic Memory Test; MBI, Modified Barthel Index; fNIRS, functional Near-infrared Spectroscopy

sensation. At the conclusion of the tDCS treatment, the current decreases gradually to 0 mA over 30 s. The total treatment duration for 1.5 mA direct current is 20 min. The virtual reality training comprises three modules: (1) Shooting the balloon, where patients controlled the handle to shoot the balloons descending from the top of the screen; (2) Shopping in the supermarket, requiring patients purchase goods and checkout in a simulated supermarket environment; (3) Looking for daily necessities, where patients enter a simulated room and were tasked with findings keys, cell phones, wallets, etc. Each training program lasts for 5 min, with 2 minutes rest interval after the end of each program, and various background music played during the training. tDCS is administered concurrently with VR, with each session lasting 20 min, conducted five times a week for four weeks.

Group B: tDCS + sham VR

Participants in this group will receive tDCS treatment d of and sham VR training. For sham VR, patients wear glasses to passively view four items without engaging in any tasks. The duration of sham VR training is consistent with the VR treatment duration.

Group C: sham tDCS + VR

Subjects in this group will undergo sham tDCS and virtual reality training. For sham tDCS, the current is gradually increased to 1.5 mA within the first 30 s, after which tDCS is discontinued. The electrode position and treatment duration are consistent with true stimulation.

Group D: sham tDCS + sham VR

Subjects in this group will receive sham tDCS and sham VR treatment. The treatment procedures are the same as before.

Criteria for discontinuing allocated interventions

1) Those who did not complete the test and quit halfway;
2) Failure to follow the prescribed protocol for treatment, or participation in other treatment studies that make it impossible to determine the efficacy of treatment;
3) Severe adverse events and complications.

Strategies to improve adherence to interventions

The interventionist encourages participants to take part in the program components. If the participant is unable to participate in a particular intervention, the researcher will contact him.

Relevant concomitant care permitted or prohibited during the trial

Subjects participating in another study while on the project will be discontinued from the study.

Outcome measurements

To assess poststroke cognitive impairment symptoms, we selected outcome measures focusing on cognition to gauge improvement in both cognitive and non-cognitive functions. All measurements will be conducted under supervision, and data will be collected by trained professionals or physicians. Index results will be evaluated before treatment and 4 weeks after treatment (Table 1).

Demographics and medical data

Demographic and clinical data will be collected at baseline using a case report form (CRF) and electronic medical records. During face-to-face interactions with patients, information such as age, sex, marital status, education level, occupational status, handedness, and stroke-related characteristics will be gathered.

Primary outcome

The Mini-Mental State Examination (MMSE) serves as a widely employed cognitive screening scale, utilized both domestically and internationally. Comprising a total score of 30 points, a score of ≤26 suggests cognitive disorder, with specific thresholds for illiteracy≤17, primary school education≤20, and junior high school and above ≤24. The MMSE encompasses six key items: orientation, attention, computation, memory, language, and visual-spatial [30]. Severity categorization is established

by MMSE scores designating≤9 points for the severe group, 10–20 points for the moderate group, and 21–26 points for the mild group. The scale's standardized, simplicity, and convenience render it apt for large-scale screening. Moreover, its sensitivity to memory and language, coupled with high sensitivity and specificity for dementia diagnosis, enhance its diagnostic utility [31]. As a primary outcome indicator, we will focus on changes in mean score on MMSE before and after treatment for post-stroke patients.

Secondary outcome

The Montreal Cognitive Assessment (MoCA) functions as a brief cognitive screening tool, demonstrating high sensitivity and specificity in detecting mild cognitive impairment (MCI) [32]. Comprising items encompassing executive functioning, language, orientation, computation, abstract thinking, memory, visual perception, attention, and concentration. The MoCA yields a total score of 30 points, where higher scores indicate superior overall cognitive function.

The Frontal Assessment Battery (FAB) proves valuable for the assessment of frontal lobe function. This tool, known for its user-friendliness and sensitive to frontal lobe malfunction, comprises six subtests: conceptualization, mental flexibility, motor programming, sensitivity to interference, inhibitory control, and environmental autonomy [33]. The FAB's total score, rate out of 18, correlates with better frontal lobe function as scores increase.

The Clock Drawing Test (CDT) is applied to evaluate subjects' visuospatial ability. This test boasts advantages such as a short assessment time, convenient scoring, patient accept ability, language, education level and cultural, background independence, as well as high sensitivity and specificity, and high predictive validity [34, 35]. The measurement is based on the internationally used 4 - point scale, with the following criteria: 1 point for drawing a closed circle (dial), 1 point for placing the digits in the correct position on the dial, 1 point for placing the 12 digits on the dial correctly, and 1 point for placing the pointer in the correct position.

The Digital Span Test (DST) serves as a tool for evaluating subjects' attention. DST comprise two subtests: Digit Span Forward and Digit Span Backward [36]. In compliance with the Digit Span Forward requirement, participants recall a series of randomly presented single digits in the order of presentation. The digit sequence varies in length, ranging from three to twelve digits. In contrast, in adherence to the Digit Span Backward requirement, participants recall the randomly single digits in reverse order. The digit sequence for this subtest ranges in length from two to ten. The maximum score is 12 points for forward and 10 points for backward, with higher scores indicative of enhance attention.

The Logic Memory Test (LMT) is employed to evaluate subjects' memory encompassing immediate and delayed memory. Subjects are tasked with recounting the content of three short stories narrated by the tester. A score of 9 or higher signifies good memory function.

The Modified Barthel Index (MBI) is utilized for assessing subjects' activity of daily living. It is recommended for both clinical and research applications due to its superior test-retest reliability and relatively lower random measurement error compared to the Barthel Index (BI) [37]. The MBI comprises 10 items as follows: grooming and bathing (five points each); feeding, toilet use, stair climbing, dressing, bowel management, and bladder management (10 points each); and chair/bed transfer and mobility (15 points each).

The apparatus S-YYZ-01, designed for diagnosis and treatment of language disorders (S-YYZ-01, ChangZhou QianJing Rehabilitation Co., LTD, China), is employed to assess subjects' speech function. The test is carried out by means of auditory examination, visual examination, speech examination, oral expression, 4sections with 65 questions, which requiring patients to respond to questions regarding question understanding, yes/no responses, phonetic/semantic expression, phonetic/semantic retelling, naming, listening, and reading words, among other tasks. The apparatus S-YYZ-01 can automatically analyze and present a variety of indicators, including oral expression, oral fluency, correct rate of speech, maximum and minimum speech energies, average speech energy, average speed of speech, and correct rate of clear and turbid tones. Each item carries a maximum score of 100, with higher score denoting superior function.

The functional near-infrared spectroscopy (fNIRS) (NirSmartII-3000 A, Danyang HuiChuang Medical Equipment Co., Ltd., Danyang, China) is a 64-channel device comprising 16 light source probes and 24 detector probes with a sampling frequency of 11 Hz. We use it to observe changes in HbO and HbR in the cerebral cortex and measure frontal cortex activities before and after cognitive training, as previously described [27]. Oxy-Hb and Deoxy-Hb concentrations in the prefrontal cortex are collected during the verbal fluency test (VFT), which is consisted of three parts. In the waiting period, patients are required to count from 1 to 5 for 30 s. During the task period, patients form words using Chinese characters appearing every 20 s, totaling 3 characters. In the later stage of the task, patients resume counting from 1 to 5 for 70s. The VFT task is presented via computer. When the first phrase task begins, the near-infrared signal will be triggered and corresponding VFT data will

be marked. The VFT cycle repeats three times in a quiet environment.

Data management and analysis data management

Upon enrollment, participants' names will be replaced with a four-letter code to protect privacy. Paper-form data will be stored in the Case Report Form (CRF) encompassing demographics, medical data, baseline, post-treatment evaluation, and record of adverse events. These data will be securely stored at the Department of Rehabilitation Medicine, The First Affiliated Hospital of Fujian Medical University. Electronic data will be deposited in the Research Manager (ResMan) database.

Data Analysis

fNIRS data preprocessing

The functional Near-Infrared Spectroscopy data will be processed using NirSpark software package v1.7.3 (Danyang HuiChuang Medical Equipment Co., Ltd., Danyang, China) [38]. First, the raw data is converted to optical density signals, with motion artifacts reduced using 3-sample interpolation. Next, the obtained signals are band-pass filtered (0.01–0.2 Hz) according to Butter's law to eliminate physiological noise generated by heartbeat, respiration, and so on. Finally, relative concentration changes of HbO, HbR, and HbT are then calculated via the Beer-Lambert law.

Statistical analysis

All data will undergo input and analysis through SPSS26.0 (IBM Corp., Armonk, USA) statistical software. The Shapiro-Wilk test and Levene test will be used to test were employed to assess the conformity of data indicators to a normal distribution and the variance across four groups. The results of the data will present as mean ± standard deviation. In cases where the data deviate from a normal distribution or exhibit uneven variance, non-parametric Mann - Whitney U test will be conducted. For data adhering to the normal distribution, we will utilize General Linear Model univariate test. The impact of tDCS and/or VR treatment cognitive function will be assessed using repeated ANOVA, with Multiple comparisons conducted through Bonferroni post-hoc test. Statistical significance will be considered when the power is less than 0.05 at the test level: $\alpha = 0.05$.

For granting public access to the full protocol, participant-level dataset

The corresponding author will provide access to the anonymized data upon reasonable request.

Data monitoring

Access to all results will be granted to the principal investigator (PI) and other project members. Additionally, the Branch for Medical Research and Clinical Technology Application, Ethics Committee of the First Affiliated Hospital of Fujian Medical University, will supervise all aspects of the study, including Adverse Events (AEs), Serious Adverse Events (SAEs), protocol bias, and progress.

Adverse events

Serious adverse events encompass incidents that are life-threatening or result in death, hospitalization (or prolongation of hospitalization), incapacity or disability [39]. Minor adverse events include new or progressive pain, non-injurious falls, severe dyspnea, worsening fatigue, palpitations, neurological deficits, altered cognitive status [39]. Adverse reactions associated with transcranial Direct Current Stimulation include headache, itching, dizziness, burning, skin redness, neck pain, inattention, and other symptoms [40].

Several measures will be implemented to prevent adverse events and monitor them: (1) All patients will be under the supervision of the therapist, and every adverse event will be meticulously recorded on the CRF. (2) Before commencing the training intervention, experimental interventionists will undergo first aid training, acquiring skills such as cardiopulmonary resuscitation (CPR). (3) During and after each treatment, experimental interventionists will inquire about adverse reactions and patient tolerance. If the patient cannot tolerate the above adverse reactions, the treatment will be discontinued. (4) Any severe adverse event will be promptly reported to the lead investigator of the trial and the Ethics Committee of the First Affiliated Hospital of Fujian Medical University within 24 h.

Dissemination policy

The results of the study will be published in scientific conferences and/or peer-reviewed journals.

Discussion

This randomized, single-center study investigates the effects of combining tDCS and VR for PSCI. We hypothesize that the combination of tDCS and VR can more effectively improve the cognitive function, speech ability, daily living ability of PSCI patients and enhance cortex activity for frontal regions compared with tDCS or VR monotherapy. This randomized study may provide a bust theoretical basis for the clinical application of tDCS-VR and offer a safe and effective strategy for treatment of PSCI.

Most of the research involving adjunctive VR and tDCS has concentrated on stimulating the motor cortex to address conditions such as cerebral palsy, pain disorders and stroke rehabilitation. The findings suggest that the combined application of these technologies yields

superior results compared to the use of either technology in isolation [41–43]. Noteworthy outcomes in body sway, gait, stroke recovery, pain management, cognitive function, and vegetative reactions have been observed in intervention groups across various demographics [22, 44]. Additionally, a meta-analysis encompassing 20 randomized controlled trials supports the notion that tDCS, when combined with rehabilitation, particular occupational therapy/physical therapy and virtual reality therapy, may benefit upper extremity function of the paretic upper limb of stroke patients [45].

To the best of our knowledge, no studies have investigated the application of combined tDCS and VR to improve cognitive function in PSCI patients. Thus, the use of tDCS with VR rehabilitation intervention emerges as a promising approach with diverse positive effects, potentially serving as an alternative to traditional rehabilitation programs for patients with PSCI.

Despite favorable data may generate from this trial involving PSCI patients, it is crucial to acknowledge certain limitations. Firstly, this is a single-center experiment, and its outcomes may not be fully representative of broader regional populations. Secondly, PSCI is heavily related to regions of the brain damage, the primary outcome measured by the MMSE may necessitate robust data support from a large sample size.

Conclusion

Amidst the prevailing trend of increasing morbidity and mortality in patients with PSCI, there is a compelling need to develop treatments that can ameliorate the condition and exert lasting effects. This randomized study may provide a scientific and bust theoretical foundation for the clinical application of tDCS-VR, offering a safe and effective strategy for the rehabilitation of PSCI patients.

Abbreviations

PSCI post	stroke cognitive impairment
tDCS	transcranial direct current stimulation
VR	virtual reality
tDCS-VR	combining tDCS and VR
MMSE	Mini-Mental State Examination
MOCA	Montreal Cognitive Assessment
FAB	Frontal Assessment Battery
CDT	Clock Drawing Test
DST	Digital Span Test
LMT	Logic Memory Test
MBI	Modified Barthel Index
fNIRS	functional Near-infrared Spectroscopy
HbO	oxygenated hemoglobin
HbR	deoxy-hemoglobin
HbT	total hemoglobin

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Author contributions

XPC, ZDW, YZZ, LL and XYC designed the study and wrote the protocol. YZZ, LQZ, DW recruited the patients. LLX, KLL, JPH collected the clinical and fNIRS data. XPC and ZDW contributed to product image data. XPC and ZDW analyzed the data. WL, JN, LL, and XYC revised the manuscript. All authors read and approved the final manuscript.

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Data availability

The corresponding author will provide access to the anonymized data upon reasonable request. For the data from this study please contact XYC.

Declarations

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Ethics statement

The study involving human participants was reviewed and approved by Branch for Medical Research and Clinical Technology Application, Ethics Committee of the First Affiliated Hospital of Fujian Medical University (Approval No.: MRCTA, ECFAH of FMU [2021]217). Informed consent will be signed after the subjects have been screened to meet the inclusion and exclusion criteria. Details of the patient's identity will not be disclosed in any publication.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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