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Title: Randomized, Triple-Blind, and Parallel-Controlled Trial of Transcranial Direct Current Stimulation for Cognitive Rehabilitation after Stroke

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Author Questionnaire

- **1. Microscopy**: Does your protocol require the use of a dissecting or stereomicroscope for performing a complex dissection, microinjection technique, or something similar? **Yes**
- **2. Software:** Does the part of your protocol being filmed include step-by-step descriptions of software usage? **YES, all done**

If Yes, we will need you to record using screen recording software.

We recommend using the screen capture program <u>OBS</u>. JoVE's tutorial for using OBS Studio is provided at this link: https://review.jove.com/v/5848/screen-capture-instructions-for-authors?status=a7854k

As these files are necessary for finalizing your script, please upload all screen-captured video files to your project page as soon as possible https://review.jove.com/account/file-uploader?src=20681793

3. Filming location: Will the filming need to take place in multiple locations? No.

Current Protocol Length

Number of Steps: 27 Number of Shots: 55



Introduction

Videographer: Obtain headshots for all authors available at the filming location.

REQUIRED:

- 1.1. <u>Begoña González Rodríguez</u>: We study the efficacy of combining tDCS with computerized cognitive stimulation in the treatment of hemispatial neglect in comparison to cognitive stimulation alone, aiming to enhance stroke cognitive rehabilitation outcomes.
 - 1.1.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera.

What are the most recent developments in your field of research?

- 1.2. <u>Elena M. Marrón</u>: Scientific evidence shows that conventional tDCS improves hemispatial neglect after stroke, with long-term benefits, but there is no evidence about the impact of high definition tDCS combined with cognitive rehabilitation.
 - 1.2.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera.

What technologies are currently used to advance research in your field?

- 1.3. <u>Marcos Rios Lago</u>: While technology is common in other rehabilitation areas, cognitive intervention has yet to fully adopt it, though digitalization and artificial intelligence are expected to enhance its protocols.
 - 1.3.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera.

What research gap are you addressing with your protocol?

- 1.4. <u>Francisco Sánchez Cuesta:</u> This protocol addresses the lack of evidence on the efficacy and focal benefits of high-definition tDCS combined with cognitive rehabilitation for treating post-stroke hemispatial neglect.
 - 1.4.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera.

will your laboratory focus on in the future?

1.5. <u>Juan Pablo Romero Muñoz:</u> Future research will explore tDCS-based neuromodulation for pain and fatigue in brain injury, multiple sclerosis and post-COVID syndrome, integrating findings from neurodegenerative diseases, clinical and neurophysiological biomarkers, and remote intervention protocol.



1.5.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera.

Videographer: Obtain headshots for all authors available at the filming location.



Ethics Title Card

This research has been approved by the Clinical Research Ethics Committee of 12 de Octubre Hospital.



Protocol

2. Setup and Execution of Cognitive and Stimulation-Based Assessment Tasks

Demonstrator: Begoña González Rodríguez

- 2.1. To begin, explain the test to the participant and ask them to follow the test instructions [1]. Confirm that the total score is greater than or equal to 24 points to proceed [2].
 - 2.1.1. WIDE: Talent seated in front of participant, explaining the test using clear gestures.
 - 2.1.2. Talent reviewing and confirming the participant's score on a printed or digital score sheet.
- 2.2. For the line bisection and Bells test, place the task centered in front of the participant [1], and indicate on the sheet the right and left sides from the participant's perspective [2]. Explain the test and ask the participant to follow the instructions [3].
 - 2.2.1. Talent positioning the task sheet on the table.
 - 2.2.2. Talent pointing to the left and right sides clearly.
 - 2.2.3. Talent verbally explaining the task while the participant listens attentively.
- 2.3. To administer the picture drawing subtests of the Barcelona test, place the task in front of the participant [1]. Point to the pictures that appear [2]. After explaining the test, have the participant follow the instructions [3].
 - 2.3.1. Shot of the task being placed in front of the participant.
 - 2.3.2. Talent pointing to the pictures.
 - 2.3.3. Shot of the participant performing the test.
- 2.4. To administer the cancellation subtests of the Barcelona test, place the task in front of the participant and indicate the right and left sides of the participant on the sheet [1]. Have the participant follow the test instructions [2].
 - 2.4.1. Talent placing test in front of participant and indicating sides on the sheet.
 - 2.4.2. Shot of the participant performing the test.
- 2.5. For the digit span forward and backward tests, verbally administer the direct digit task [1]. Then, administer the inverse digits task [2].
 - 2.5.1. Shot of participant responding verbally to the direct digit task.
 - 2.5.2. Shot of participant responding verbally to the indirect digit task.



- 2.6. To administer the brief test of attention, first administer the verbal part of the first task by asking the participant to count the numbers that appear in sequence [1]. Then ask the participant to immediately apply the second part which is to count the number of letters that appear in the sequence [2].
 - 2.6.1. Shot of the participant verbally counting the numbers that appear in the sequence.
 - 2.6.2. Shot of the participant counting the letters that appear in the sequence.
- 2.7. For the face test, present the face test sheet to the participant [1]. Explain the test and ask them to follow the instructions [2].
 - 2.7.1. Talent placing the face test sheet on the table in front of the participant.
 - 2.7.2. Talent providing verbal instructions as participant nods in understanding.
- **2.8.** For the Motor-free visual perception test, place the homework notebook in front of the participant [1]. Explain the test and ask them to follow the instructions [2].
 - 2.8.1. Talent positioning the notebook in front of the participant.
 - 2.8.2. Shot of the participant performing the test.
- 2.9. To know the patient's functional status, administer the Barthel Index scale to the family member or primary caregiver [1]. Record their responses on the answer sheet [2]. Then administer the Catherine Bergego Scale to the family member or primary caregiver and record responses on the answer sheet [3].
 - 2.9.1. Talent reading questions aloud to the patient's family member/ primary caregiver.
 - 2.9.2. Talent recording responses on the answer sheet.
 - 2.9.3. Talent administering the CBS and marking responses clearly.

3. Administration of Transcranial Direct Current Stimulation (tDCS) with Neurorehabilitation Activities

Demonstrator: Francisco Sánchez Cuesta

- **3.1.** To configure the intervention device, first launch the software, select **Protocol Editor**, add a new protocol and enter the name of the protocol [1].
 - 3.1.1. SCREEN: 67809_-screenshot_1.mp4 00:00-00:14
- 3.2. Confirm the ramp and total stimulation time by indicating Ramp-Up: 30 (Ramp-Up-Thirty) and Ramp-Down: 30 (Ramp-Down--Thirty) [1]. In the total stimulation duration section, indicate 20 minutes and press the Sham button if it corresponds to the condition [2].

3.2.1. SCREEN: 67809_-screenshot_1.mp4 00:15-00:20 3.2.2. SCREEN: 67809 -screenshot 1.mp4 00:21-00:26



- **3.3.** Then select the stimulation program to begin configuring the **tDCS** (*T-D-C-S*) and **Basic** electrodes that will be part of the setup configuration [1].
 - 3.3.1. SCREEN: 67809 -screenshot 1.mp4 00:27-00:31
- **3.4.** Then select electrode P3 and drag it to the box on the right. Choose **stimulation** and **cathodal**, and enter 2000 microamperes [1]. Then, select and drag to the left and space the return electrodes one by one, indicating the return percentage for each [2]. Click the **Finish** button once complete [3].
 - 3.4.1. SCREEN: 67809 -screenshot 1.mp4 00:32-00:40
 - 3.4.2. SCREEN: 67809_-screenshot_1.mp4 00:40-00:45,00:50-00:52, 01:25-
 - 01:35
- 3.5. Assess the level of mental fatigue and mood using two self-administered VAS (V-A-S) scales [1-TXT]. Ask the participant to provide a score from 1 to 10 for each question, where 1 is the lowest mental fatigue, and lowest mood respectively [2].
 - 3.5.1. Talent handing over VAS sheets. TXT:VAS: Visual Analog Scales
 - 3.5.2. Shot of participants verbally answering the questions.
- 3.6. Next, place the active cathode electrode at P3 (*P-Three*) and return electrodes at C3(*C-Three*), CP5 (*C-P-Five*), CP1 (*C-P-One*), Pz (*P-Zee*), PO3(*P-Oh-Three*), PO7(*P-Oh-Seven*), and P7 (*P-Seven*) on the neoprene cap [1].
 - 3.6.1. Talent identifying and placing each electrode at the specified positions.
- **3.7.** After placing the lower part of each electrode in the selected areas, put the cap on the participant's head and adjust Cz (*C-Zed*) based on prior measurements [1]. Next, seat the participant in a comfortable position in a chair [2].
 - 3.7.1. Talent fitting and adjusting the cap on participant's head. Videographer's NOTE: 3.7.1 + 3.7.2 Shot together.
 - 3.7.2. Talent placing the participant in a comfortable position on a chair.
- **3.8.** After putting on a neoprene cap on the participant's head, adjust it using the headband until the cap fits snugly [1]. NOTE: The VO has been edited.
 - 3.8.1. Talent placing appropriate neoprene cap on the participant's head. Videographer's NOTE: Removed Shot 3.8.1
 - 3.8.2. Talent tightening the headband for a secure fit.
- 3.9. Locate the Cz point and the stimulation zones of the protocol [1].
 - 3.9.1. Talent pointing to Cz and verifying all electrode placements.



- **3.10.** Then measure the distance between nasion and inion and between the preauricular points using a meter [1]. Locate Cz at the midpoint of both measurements [2].
 - 3.10.1. Talent using a flexible measuring tape. Videographer's NOTE: 3.10.1 + 3.10.2 Shot together.
 - 3.10.2. Talent marking Cz accurately.
- **3.11.** Separate the hair under each electrode using an elongated object to ensure good contact without disturbing cap placement [1]. Now, using a syringe with a plastic tip, introduce sufficient electroconductive gel at the base of each electrode [2].
 - 3.11.1. Talent carefully lifting hair strands from under electrodes.
 - 3.11.2. Talent injecting gel precisely into each electrode site.
- **3.12.** Turn on the tDCS (*T-D-C-S*) device [1] and launch the software on the computer [2].
 - 3.12.1. Talent turns on the tDCS device. **TXT: tCDS: transcranial Direct Current**Stimulation
 - 3.12.2. SCREEN: 67809 -screenshot 2.mp4 00:02-00:09
- 3.13. Choose the connection used with the device and select the Scan for device option [1]. Press Load Protocol then click on Check Impedance [2]. If all electrodes appear green, press the Play button to start the stimulation program [3-TXT].

3.13.1. SCREEN: 67809 -screenshot 3.mp4 00:02-00:04, 00:09-00:15

3.13.3. SCREEN: 67809_-screenshot_3.mp4 01:20-01:32 **TXT:** If any electrode appears red, reapply gel, remove hair and recheck impedance

3.14. Next, access the computerized neurorehabilitation platform [1]. Access the planned session and press **Start** [2]. Present four stimulation activities of 7 minutes each sequentially and assign the task to the participant in the calendar [3].

3.14.2. SCREEN: 67809 -screenshot 4.mp4 00:19-00:30

01:24,01:40-01:42, 02:05-02:14

Video Editor: Please speed up the video if necessary

3.15. Activate tDCS stimulation by pressing **Play** on the control software 4 minutes and 20 seconds after starting the neurorehabilitation task **[1]**.

3.15.1. SCREEN: 67809 -screenshot 5.mp4 00:00-00:14

3.16. Afterwards, apply an adapted Questionnaire of Sensations Related to Transcranial Electrical Stimulation. Ask 9 questions about symptoms such as headache, scalp burning, and tingling **[1]**. Re-administer the VAS scale used before the stimulation to evaluate fatigue and mood after intervention **[2]**.



3.16.1. Talent verbally administering the questionnaire while participant responds.

AND

Table 3

Video Editor: Please show both shots side by side

- 3.16.2. Talent handing over VAS sheet again and guiding participant.
- **3.17.** Once the tDCS stimulation program and neurorehabilitation tasks are finished, close the tDCS software [1]. Disconnect the tDCS device [2]. Remove the cable that connects the tDCS with the electrodes [3]. Then remove the cap from the participant's head [4].
 - 3.17.1. SCREEN: 67809_-screenshot_6.mp4 00:00-00:19
 - 3.17.2. Talent unplugging the device from power and computer.
 - 3.17.3. Talent gently detaching cables from electrodes.
 - 3.17.4. Talent lifting the neoprene cap and placing it aside.



Results

4. Results

- **4.1.** In the post-intervention assessment quantitative changes were observed in 6 of the 13 tests administered, 4 of which are directly related to neglect [1].
 - 4.1.1. LAB MEDIA: Table 4 and Figure 8 *Video Editor: Please highlight the columns corresponding to "post-intervention" in both figure and table*
- **4.2.** Clinical improvement was observed in the specific hemispatial neglect tests[1]. On the other hand, negative changes were observed in other attentional tasks [2].
 - 4.2.1. LAB MEDIA: Figure 9 Video Editor: Please highlight the columns corresponding to bells test, cancellation test, line bisection, visual motor-free perception test, and Barthel index scale
 - 4.2.2. LAB MEDIA: Figure 9 *Video Editor: Please highlight the columns corresponding to digit test, brief test of attention, face test*

Pronunciation Guides:

1. Electroconductive

Pronunciation link:

https://www.merriam-webster.com/dictionary/electroconductive

IPA (American): /ɪˌlɛktroʊkənˈdʌktɪv/

Phonetic Spelling: ih-lek-troh-kuhn-duk-tiv

2. Transcranial

Pronunciation link:

https://www.merriam-webster.com/medical/transcranial

IPA (American): /træns'kreɪniəl/ Phonetic Spelling: trans-kray-nee-uhl

3. Stimulation

Pronunciation link:

https://www.merriam-webster.com/dictionary/stimulation

IPA (American): /ˌstɪmjəˈleɪʃən/
Phonetic Spelling: stim-yuh-lay-shun

4. Rehabilitation



Pronunciation link:

https://www.merriam-webster.com/dictionary/rehabilitation

IPA (American): /ˌriː(h)əˌbɪlɪˈteɪʃən/
Phonetic Spelling: ree-huh-bil-ih-tay-shun

5. Index

Pronunciation link:

https://www.merriam-webster.com/dictionary/index

IPA (American): /'ɪnˌdɛks/ Phonetic Spelling: in-deks

6. Scale

Pronunciation link:

https://www.merriam-webster.com/dictionary/scale

IPA (American): /skeɪl/ Phonetic Spelling: skayl

7. Electrode

Pronunciation link:

https://www.merriam-webster.com/dictionary/electrode

IPA (American): /ɪˈlɛktroʊd/ Phonetic Spelling: ih-lek-trohd

8. Impedance

Pronunciation link:

https://www.merriam-webster.com/dictionary/impedance

IPA (American): /ɪmˈpiːdəns/
Phonetic Spelling: im-pee-duhns

9. Protocol

Pronunciation link:

https://www.merriam-webster.com/dictionary/protocol

IPA (American): /ˈproʊtəˌkɔl/ Phonetic Spelling: proh-tuh-kawl

10. Electrode

Pronunciation link:

https://www.merriam-webster.com/dictionary/electrode

IPA (American): /ɪˈlɛktroʊd/ Phonetic Spelling: ih-lek-trohd