FINAL SCRIPT: APPROVED FOR FILMING

Submission ID #: 67888
Scriptwriter Name: Sulakshana Karkala
Project Page Link: https://review.jove.com/account/file-uploader?src=20705888

Title: Localizing Function-Specific Targets for Transcranial Magnetic Stimulation in the Absence of Navigation Equipment

Authors and Affiliations:
Bingbing Zhou[1*], Jiajia Qi[1*], Kangjia Chen[2*], Hong Li[1], Jiahui Liu[1], Qian Zhou[1], Zujuan Ye[1], Jue Wang[1]

[1]Chengdu Sport University
[2]University of Electronic Science and Technology of China

***These authors contributed equally**

Corresponding Authors:
Jue Wang (juefirst@cdsu.edu.cn)
Email Addresses for All Authors:
Bing-Bing Zhou (zhoubingbing199905@163.com)
Jia-Jia Qi (qijiajia0629@163.com)
Kang-Jia Chen (chenkangjia_uestc@163.com)
Hong Li (lh18360937396@163.com)
Jia-Hui Liu (keyi877176272@163.com)
Qian Zhou (zhouqian001210@163.com)
Zu-Juan Ye (yzujuan@163.com)
Jue Wang (juefirst@cdsu.edu.cn)

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? No

2. Software: Does the part of your protocol being filmed include step-by-step descriptions of software usage? **Yes**

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

Current Protocol Length
Number of Steps: 27
Number of Shots: 50

Introduction

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

REQUIRED:

1.1. **Jue Wang:** I work in motor cognitive neuroscience, looking at how to boost fine hand movements with TMS. We're trying to find simple ways to target the brain function, even without navigation systems.

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. **Bingbing Zhou:** Transcranial Magnetic Stimulation targeting has gone from simple spot-picking to tuning brain networks, and with AI helping, it's getting smarter, more personal, and closer to custom brain treatments.

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. **Jiajia Qi:** Right now, ways to define Transcranial Magnetic Stimulation targets include multimodal imaging-guided, fMRI-guided, picking targets based on cognitive performance, using closed-loop and brain-state dependent TMS, and modeling electric fields with high precision.

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

What are the current experimental challenges?

1.4. **Kangjia Chen:** It is challenging to map 3D cortical coordinates onto the 2D scalp without introducing errors.

1.4.1. 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?

1.5. **Hong Li:** Most clinics don't have neuronavigation systems, so they cannot offer personalized, function-specific Transcranial Magnetic Stimulation treatments. Our protocol solved this problem.

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.

Testimonial Questions:

How do you think publishing with JoVE will enhance the visibility and impact of your research?

1.6. **Jue Wang:** Publishing in JoVE is likely to increase our clinical collaborations and citation counts. It will also reduce the manpower required for training after publication. Additionally, our ruler will help clinics save on the costs of navigation equipment.

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

AUTHORS: Please deliver the interview statements in both Chinese and in English

Ethics Title Card

This research has been approved by the Ethics Committee at Chengdu Sport University

Protocol

2. Functional Localization and Stimulation Targeting Workflow for Task-State fMRI Analysis

Demonstrator: Bingbing Zhou

2.1. To begin, open the preprocessing software **[1]**. Click on **DPARSF 5.4** *(D-P-A-R-S-F-five-point- four)*, then choose the **DPARSF Advanced Edition** to preprocess the task-state data using specific parameters **[2]**.

2.1.1. WIDE: Talent launching the DPARSF software.

2.1.2. SCREEN: 67888_screenshot_1.mp4 00:00-00:06

2.2. Perform slice timing and head motion corrections. Coregister the functional images to structural images and apply spatial smoothing with a full width at half maximum of 6 millimeters **[1]**.

2.2.1. SCREEN: 67888_screenshot_1.mp4 00:07- 00:52

2.3. Open SPM12 *(S-P-M-Twelve)* and click on **Coregister Estimate [1]**. For the **Reference Image**, select the file named **sub *crop_1.nii** *(sub-asterisk-crop-underscore-1-dot-N-I-I)* from the T1Img *(T-one-I-M-G)* folder **[2]**. For the **Source Image**, choose the **mean*.nii** *(mean-asterisk-dot-N-I-I)* file from the RealignParameter *(Realign-Parameter)* folder **[3]**. For the **Other Image**, select the **ra*.nii** *(Rah-asterisk-N-I-I)* file from the FunImgAR *(Fun-I-m-g-A-R)* folder **[4]**.

2.3.1. SCREEN: 67888_screenshot_1.mp4 00:54-00:58, 01:04-01:10

2.3.2. SCREEN: 67888_screenshot_1.mp4 01:12-01:16

2.3.3. SCREEN: 67888_screenshot_1.mp4 01:17-01:23

2.3.4. SCREEN: 67888_screenshot_1.mp4 01:25-01:36

2.4. Click on **Segment** and then **select** Volumes. Choose the **sub*crop_1.nii** file from the T1Img folder **[1]**. For **Deformation Fields**, select **Inverse + Forward** *(Inverse plus Forward)*, then click **Run [2]**. Repeat this segmentation for the **sub*.nii** file from the same folder **[3]**.

2.4.1. SCREEN: 67888_screenshot_1.mp4 01:52-02:04

2.4.2. SCREEN: 67888_screenshot_1.mp4 02:05-02:10

2.4.3. SCREEN: 67888_screenshot_1.mp4 02:16-02:33
Video Editor: Please speed up the video

2.5. Next, click on **Smooth**. Select the **ra*.nii** files from the FunImgAR folder for **Image to Smooth** and enter **6 6 6** in the **FWHM** *(F-W-H-M)* field **[1]**.

2.5.1. SCREEN: 67888_screenshot_1.mp4 02:36-02:58

2.6. Perform first-level analysis to obtain individual activation maps and identify the peak voxel of activation as the stimulation target **[1]**.
 2.6.1. SCREEN: 67888_screenshot_1.mp4 05:36-05:46

2.7. Create a new folder named **indiv_act** *(in-div-underscore-act)* and click on **Specify 1st-level** *(Specify-first-level)* **[1]**. In the **Directory** field, select the **indiv_act** folder, click on **Units for design**, choose **Scans**, and enter **2** for the **Interscan interval [2]**.
 2.7.1. SCREEN: 67888_screenshot_1.mp4 03:48-04:03
 Video Editor: Please speed up the video
 2.7.2. SCREEN: 67888_screenshot_1.mp4 04:04-04:18

2.8. In the **Data & Design** *(Data-and-Design)* section, choose the **sra*.nii** *(S-R-A-Asterisk-dot-I-I)* files under **Scans [1]**. Under the **Condition** section, set **Name** to **tap**, then enter **0 30 60 90** *(Zero-thirty-sixty-ninety)* for **Onset**, and set **Durations** to **15 [2]**. Then click on **Multiple regressors** and select the **rp_a*.txt** *(R-P-Underscore_A-Asterisk-dot-T-X-T)* file from the **RealignParameters [3]**.
 2.8.1. SCREEN: 67888_screenshot_1.mp4 04:20-4:35, 4:47-04:58
 Video Editor: Please speed up the video
 2.8.2. SCREEN: 67888_screenshot_1.mp4 05:01-05:17
 2.8.3. SCREEN: 67888_screenshot_1.mp4 05:22-05:29

2.9. To estimate, select the **SPM.mat** *(S-P-M-Mat)* file from the **indiv_act** folder and generate the individual task activation map, spmT_0001 *(S-P-M-T-Underscore-zero-zero-zero-one)* **[1]**.
 2.9.1. SCREEN: 67888_screenshot_1.mp4 05:48-05:56

2.10. Now press **Results** and choose the **SPM.mat** file from the **indiv_act** folder, check **t-contrast** and click on **Define new contrast [1]**. Enter a custom name, then input **1 0** *(one-zero)* in the **contrast** field, and click on **Submit, OK, Done [2]**.
 2.10.1. SCREEN: 67888_screenshot_1.mp4 06:05-06:27
 2.10.2. SCREEN: 67888_screenshot_1.mp4 06:28- 06:38

2.11. Under **Apply masking**, select **None**, then choose **None** under **p value adjustment to control** and set the value **to 0.001**. Set the **&** *(and)* **extend threshold** to **0 [1]**.
 2.11.1. SCREEN: 67888_screenshot_1.mp4 06:39-06:43

2.12. Now click on **Normalise (Write)** *(Normalise-Write)* and then **Data**. In **Deformation Fields**, select the **iy_Crop_1** *(I-Y-Crop-One)* file from the **T1Img** folder **[1]**. For **Image to write**, choose the **M1 brain region mask**, then enter the individual bounding box and voxel sizes **[2]**.
 2.12.1. SCREEN: 67888_screenshot_1.mp4 08:17-08:31
 2.12.2. SCREEN: 67888_screenshot_1.mp4 08:32-08:38

2.13. Next press **Coregister Reslice**, then select **spmT_0001** from the **indiv_act** folder for **Image Defining Space**. For **Image to Reslice**, choose the w*.nii *(W-asterisk-dot-N-i-i)* file generated previously **[1]**.

2.13.1. SCREEN: 67888_screenshot_1.mp4 09:01-09:20

2.14. Now, compute the individual task activation peak. In MATLAB, run the **sort positive code** then input names as given **[1].** Identify the first X-coordinate with a negative value and record it as the individual task activation peak **[2]**.

2.14.1. SCREEN: 67888_screenshot_1.mp4 09:34-09:45, 09:58-10:01, 10:07-10:14, 10:25-10:32
AND
TEXT ON PLAIN BACKGROUND:
InputName1: select the path of the rw*.nii file
InputName2: Select the path of the spmT_0001 file from the indiv_act folder
InputName3: Select the output folder path
Video Editor: Please play both shots side by side

2.14.2. SCREEN: 67888_screenshot_1.mp4 11:08-11:15

2.15. To locate the individualized function-specific target, first determine the output intensity of the stimulator based on the participant's resting motor threshold **[1]**. Use a frameless stereotactic optical tracking neuronavigation system, with the participant seated comfortably and wearing a head-mounted calibrator **[2]**.
Videographer: Please record screens of instrument for 2.15-2.17

2.15.1. Talent determining the output intensity. Videographer's NOTE: This step involves hand movements and screen display, so I broke it down into three separate shots for filming.

2.15.2. Shot of Participant seated in a chair while a head-mounted calibrator is positioned and adjusted.

2.16. Click on the **anatomical** option. Then import the participant's T1-weighted structural images into the navigation system for head modeling **[1]**. Click on the **Reconstruction** option and reconstruct the skin on the image **[2]**.

2.16.1. Shot of the anatomical option being clicked and the Navigation software import of T1-weighted images for anatomical modeling.

2.16.2. Shot of Skin surface reconstruction process being initiated and visualized on the navigation interface.

2.17. Next, press the **Landmarks** option. Use the **localizer** tool to mark four landmarks on the participant's head **[1]**. Then click on the **Target** option. Identify and establish the target trajectory in the brain region **[2]**. Then locate the stimulation target on the participant's individual images. After positioning, move the target to align with the crosshairs and complete TMS *(T-M-S)* localization **[3]**.

2.17.1. Shot of the Localizer tool being used to define and mark the four anatomical landmarks.
2.17.2. Shot of Target being clicked. The target trajectory is being identified in the brain. Videographer's NOTE: 2.17.2 and 2.17.3 were filmed continuously, so they are in the same video.
2.17.3. Shot of the stimulation target is being located on the images. Then the target is being moved to align with the crosshairs and the TMS localization is being completed.

2.18. To locate the individualized function-specific target launch SPM12 *(S-P-M-Twelve)*, click on **fMRI** *(F-M-R-I)*, and then select **Segment** from the menu **[1]**. Under the **parameters** interface, press the **Volumes** button, select the **MNI** *(M-N-I)* brain **template file**, then click on **Deformation Fields** to select **Inverse + Forward [2]**.
2.18.1. SCREEN: 67888_screenshot_2.mp4 00:00-00:04
2.18.2. SCREEN: 67888_screenshot_2.mp4 00:04-00:22

2.19. Next, launch MATLAB and run the edges code to outline the inner and outer edges of the standard scalp. Select the **c5.nii** image, then click **Done** to generate the **c5_edges.nii** file **[1]**.
2.19.1. SCREEN: 67888_screenshot_2.mp4 00:31- 01:07
Video Editor: Please speed up the video

2.20. Now use SPM12 to transform the standard scalp edge into individual space. Click **Normalise (Write)** and click on **Data [1]**. Select the **iy_sub*.nii** file from the T1Img folder under **Deformation Fields**. Choose **c5_outer_edge.nii** for **Images to Write** and input the individual bounding box and voxel sizes **[2]**.
2.20.1. SCREEN: 67888_screenshot_2.mp4 01:12-01:20
2.20.2. SCREEN: 67888_screenshot_2.mp4 01:21-01:38, 01:40-2:18

2.21. Convert cortical coordinates to scalp coordinates by opening the **TransCortex2Scalp** *(Trans-Cortex-two-Scalp)* code in MATLAB and execute the first line. Enter the individual activation point coordinates, select the wc5_outer_edge.nii *(W-C-Five-Outer-Edge)* file, then record the output coordinates **[1]**.
2.21.1. SCREEN: 67888_screenshot_2.mp4 02:51-03:14

2.22. Open **DPABI_Viewer** *(D-Pahbee-Viewer)*, click on **Underlay** and select the individual T1 structural image **[1]**. Locate and record the coordinates of the left and right auricular peaks, the nasion, and the inion **[2]**.
2.22.1. SCREEN: 67888_screenshot_2.mp4 03:30-03:42
2.22.2. SCREEN: 67888_screenshot_2.mp4 03:46-04:10, 04:20-04:26, 04:40-04:47
Video Editor: please speed up the video, if needed

2.23. Now, define the scalp origin by opening the **intersection** code in MATLAB. Input the coordinates of the four landmark points, then run the code to calculate the intersection coordinates of the ear and nasion-inion lines. Record the intersection coordinates **[1]**.

2.23.1. SCREEN: 67888_screenshot_3.mp4 00:00-00:20

2.24. To move the intersection point along the Z-axis to the scalp, open the origin code in MATLAB, enter the intersection point coordinates in **Define point H**, and select the **wc5_outer_edge.nii** file. Obtain the scalp origin coordinates O **[1]**.

2.24.1. SCREEN: 67888_screenshot_3.mp4 00:21-00:40

2.25. To calculate the actual distance from the scalp origin to each point, run the **distance** code, select the **wc5_outer_edge.nii** file, and enter the scalp origin, target, and four landmark point coordinates as prompted **[1]**.

2.25.1. SCREEN: 67888_screenshot_3.mp4 00:44-00:59, 01:06-01:11, 01:15-01:30

2.26. Now, calculate the angle between the line connecting the scalp target and the scalp origin and the X-axis in the XY plane by opening the **calculate_angle_X_axis** *(calculate-angle-X-axis)* code and run the first line **[1]**. In the **command** window, input the coordinates of the scalp origin and stimulation target **[2]**.

2.26.1. SCREEN: 67888_screenshot_3.mp4 01:32-01:36

2.26.2. SCREEN: 67888_screenshot_3.mp4 01:35-02:07

2.27. Use the targeting ruler to fix the corresponding soft ruler position based on the calculated distance and angle **[1]**. Then mark the scalp with a washable pen **[2]**.

2.27.1. Talent aligning soft ruler on the scalp using targeting measurements.

2.27.2. Talent marking the stimulation site with a pen.

Results

3. Results

3.1. Based on one-sample t-test maps, functional connectivity **[1]** and amplitude of low-frequency fluctuation results are displayed without multiple comparison correction **[2].**

3.1.1. LAB MEDIA: Figure 5 *Video Editor: Please highlight the first row*

3.1.2. LAB MEDIA: Figure 5 *Video Editor: Please highlight the second row*

Pronunciation Guides:

1. SPM12

- **Pronunciation link:** No confirmed link found
- **IPA:** /ɛs piː ɛm twɛlv/
- **Phonetic Spelling:** ess-pee-em twelve

2. MATLAB

- **Pronunciation link:** https://www.howtopronounce.com/matlab
- **IPA:** /ˈmæt.læb/
- **Phonetic Spelling:** mat-lab

3. Voxel

- **Pronunciation link:** https://www.merriam-webster.com/dictionary/voxel
- **IPA:** /ˈvɑːk.səl/
- **Phonetic Spelling:** vok-suhl

4. Nasion

- **Pronunciation link:** https://www.howtopronounce.com/nasion
- **IPA:** /ˈneɪ.ʒən/
- **Phonetic Spelling:** nay-zhun

5. Inion

- **Pronunciation link:** https://www.howtopronounce.com/inion

- **IPA:** /ˈɪn.i.ən/
- **Phonetic Spelling:** in-ee-un

6. Auricular

- **Pronunciation link:** https://dictionary.cambridge.org/us/pronunciation/english/auricular
- **IPA:** /ɔːˈrɪk.jʊ.lər/
- **Phonetic Spelling:** aw-rik-yuh-lur

7. TMS

- **Pronunciation link:** https://www.howtopronounce.com/tms
- **IPA:** /tiː ɛm ɛs/
- **Phonetic Spelling:** tee-em-ess

8. fMRI

- **Pronunciation link:** https://www.howtopronounce.com/fmri
- **IPA:** /ˌɛf ˌɛm ɑːr ˈaɪ/
- **Phonetic Spelling:** ef-em-ar-eye

9. MNI

- **Pronunciation link:** https://www.howtopronounce.com/mni
- **IPA:** /ɛm ɛn aɪ/
- **Phonetic Spelling:** em-en-eye