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Title: Conventional Repetitive Transcranial Magnetic Stimulation for Depression: A Step-by-Step Protocol

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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? **No**

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

Videographer: Please record the device/monitor/screen for the shots labeled as SCREEN

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

4. **Testimonials (optional):** Would you be open to filming two short testimonial statements **live during your JoVE shoot**? These will **not appear in your JoVE video** but may be used in JoVE's promotional materials. **Yes**

Current Protocol Length
Number of Steps: 25
Number of Shots: 50 (5 SC)

Introduction

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

INTRODUCTION:

1.1. **Gonçalo Cotovio:** We describe conventional methods for therapeutic use of rTMS for treatment-resistant depression, through a precise and patient-centered protocol, enhancing safety, comfort, and reproducibility.

1.1.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B-roll: 2.3.1*

1.2. **Albino J. Oliveira-Maia:** Recent advances include accelerated rTMS protocols, neuronavigation-based targeting, and personalized targeting using individual-level functional brain connectivity, which are thought to improve treatment outcomes.

1.2.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B-roll: 2.5.1*

1.3. **Patrícia Pereira:** While exciting developments are occurring for the use of rTMS to treat depression, establishing even the more conventional protocols can be challenging in some settings.

1.3.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B-roll: 3.2.1* **NOTE**: This shot was erroneously marked as 1.5.1 in the shot. So, there will be two 1.5.1. The shot featuring a woman is the 1.3.1.

CONCLUSION:

1.4. **Gonçalo Cotovio:** We provided a standardized rTMS protocol that may improve treatment consistency, reliability, and comfort, supporting effective depression therapy across clinical settings.

1.4.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B-roll: 4.1.1*

1.5. **Albino J. Oliveira-Maia:** Conventional rTMS has paved the way for research focusing on optimizing stimulation parameters, refining strategies for cortical targeting and evaluating the long-term effectiveness of rTMS for depression.

1.5.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B-roll: 5.2.1*

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

NOTE: Not filmed

Testimonial Questions (OPTIONAL):

Videographer: Please capture all testimonial shots in a wide-angle format with sufficient headspace, as the final videos will be rendered in a 1:1 aspect ratio. Testimonial statements will be presented live by the authors, sharing their spontaneous perspectives.

- Testimonial statements will **not appear in the video** but may be featured in the journal's promotional materials.
- **Provide the full name and position** (e.g., Director of [Institute Name], Senior Researcher [University Name], etc.) of the author delivering the testimonial.
- Please **answer the testimonial question live during the shoot**, speaking naturally and in your own words in **complete sentences**.

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

1.6. **Gonçalo Cotovio, Psychiatrist at the Champalimaud Clinical Centre**

(authors will present their testimonial statements live)

1.6.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B-roll: 4.1.1*

Can you share a specific success story or benefit you've experienced—or expect to experience—after using or publishing with JoVE? (This could include increased collaborations, citations, funding opportunities, streamlined lab procedures, reduced training time, cost savings in the lab, or improved lab productivity.)

1.7. **Albino J. Oliveira-Maia, Director of Neuropsychiatry at the Champalimaud Foundation;** : (authors will present their testimonial statements live)

1.7.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B-roll: 5.2.1*

Authors: Could you please also deliver the above statements in Portuguese?
Videographer: Please film the testimonials in both English and Portuguese

Ethics Title Card

This protocol was used in a study approved by the Champalimaud Ethics Committee, where informed consent was obtained from all participants

Protocol

2. Determining the Motor Hotspot and Resting Motor Threshold (rMT)

Demonstrator: Francico Viana e Patrícia Pereira

2.1. To begin, place a lycra cap on the patient to mark areas of interest on the scalp **[1]**. Confirm that the cap is aligned with the patient's eyebrows and the upper part of the ears to ensure consistent reference points for future sessions **[2]**.

2.1.1. WIDE: Talent placing a lycra cap carefully on the patient's head.

2.1.2. Talent adjusting the cap, ensuring alignment with the eyebrows and upper edges of the ears.

2.2. Provide earplugs to the patient to minimize discomfort caused by stimulating sounds **[1]**. Wear your own earplugs before beginning the transcranial magnetic stimulation procedure **[2]**.

2.2.1. Talent handing a pair of earplugs to the patient and demonstrating their use.

2.2.2. Talent inserting personal earplugs into both ears.

2.3. Record all preparatory steps and safety measures in the patient's clinical chart **[1]**.

2.3.1. Talent writing notes into the patient's electronic or paper clinical record.

2.4. To determine the motor hotspot, identify the stimulation hotspot for the primary motor cortex of the hand region in the left hemisphere **[1]**.

2.4.1. Talent and patient positioned for transcranial magnetic stimulation setup.

2.5. Using a measuring tape, measure and mark the mid-sagittal line extending from the nasion, which is the top of the nose bridge, to the inion, which is the prominent bump at the back of the skull **[1]**.

2.5.1. Talent using a measuring tape to draw a straight mid-sagittal line along the scalp from the nasion to the inion.

2.6. Now, mark the intertragus line by placing one end of the measuring tape at one tragus,

which is the point just in front of the ear, and stretching it across to the opposite tragus **[1]**.

2.6.1. Talent measuring and marking a line from one tragus across the head to the other side using a measuring tape.

2.7. Identify the intersection of the mid-sagittal and intertragus lines as the cranial vertex **[1]**. Use this point as the reference from which additional measurements will be taken to locate the motor cortex hotspot **[2]**.

2.7.1. Talent marking the intersection point of the two lines on the scalp.

2.7.2. Close up of this point as the cranial vertex reference on camera.

2.8. Next, draw a triangle by extending a line 5 centimeters to the left along the intertragus line and another 5 centimeters anteriorly along the mid-sagittal line, both starting from the cranial vertex **[1]**. Connect the free ends of these two lines diagonally to form a triangle **[2]**. The starting reference point for locating the hand motor hotspot is positioned 2.5 centimeters along this diagonal line, measured from the left-most vertex of the triangle **[3]**.

2.8.1. Talent marking a line 5 centimeters to the left along the intertragus line and 5 centimeters forward along the mid-sagittal line.

2.8.2. Talent drawing a diagonal line connecting the ends of the two measured segments to form a triangle.

2.8.3. Talent marking a point 2.5 centimeters along the diagonal from the left-most vertex of the triangle.

2.9. Then, mark 4 additional points located 0.5 centimeters anterior, posterior, lateral, and medial from the reference point to allow detailed exploration during hotspot identification **[1]**.

2.9.1. Talent marking 4 equidistant points around the primary reference point on the scalp.

2.10. Use these 5 points as the designated positions where the anterior edge of the transcranial magnetic stimulation coil will be placed during the motor hotspot detection procedure **[1]**. Before initiating the search for the motor hotspot, instruct the patient to rest their arms and hands on the armrests of the chair or on their lap, ensuring that both are visible and relaxed **[2]**.

2.10.1. Talent showing the 5 marked scalp points and positioning the coil anterior edge

sequentially at each point.

2.10.2. Talent guiding and the patient relaxing their arms on the armrests, ensuring a calm posture.

2.11. Place the handle of the figure-of-eight transcranial magnetic stimulation coil on the patient's head at a 45-degree angle relative to the sagittal midline **[1]**, with the handle directed posteriorly and to the left **[2]**.

2.11.1. Talent correctly positioning the figure-of-eight coil on the patient's head at a 45-degree angle to the midline.

2.11.2. Shot of the handle pointing backward and to the left.

~~**3. Transcranial Magnetic Stimulation and Resting Motor Threshold (rMT) Determination**~~

NOTE: Do not display the section 3 title. Continue with 3.1.1 after 2.11.2 directly under the section 2

3.1. Apply transcranial magnetic stimulation pulses while maintaining the coil in the previously described position **[1]**. To help the patient become accustomed to the procedure, deliver the initial pulses at a lower intensity, approximately 20 to 30 percent of the maximum output, while assessing the patient's sensory experience **[2]**. Confirm the visible muscle contraction in the contralateral hand muscles **[3]**.

3.1.1. Talent maintaining the figure-of-eight coil over the patient's head while applying the initial stimulation pulses.

3.1.2. Talent observing and engaging with the patient to assess comfort and sensory feedback during the initial low-intensity pulses.

3.1.3. Close-up shot showing visible contraction of the contralateral hand muscles in response to stimulation.

3.2. If no motor response is observed at the initial intensities across the marked reference points, increase the stimulation intensity in 5 percent increments until a motor response, defined as a visible contraction of the right hand, is obtained **[1]**. Once a motor response is detected, test the remaining marked points to identify the location that produces the strongest contraction **[2]**.

3.2.1. Talent gradually increasing the intensity on the transcranial magnetic stimulation device.

3.2.2. Talent sequentially repositioning the coil over the various marked scalp points and observing the hand for maximum motor response. **Author's NOTE:** Please use frames from shot 2.10.1 and/or a new shot that was labeled as 2.10.3

3.3. Mark additional reference points as necessary at new positions spaced approximately 1 centimeter apart to refine the search **[1]**. Identify the motor hotspot as the point that produces the largest and most consistent muscle contraction **[2]**.

3.3.1. Talent marking new scalp positions at increased spacing from the initial set of points.

3.3.2. Close-up of the patient's hand showing the most pronounced contraction when the optimal point is stimulated. **Author's NOTE**: Please use frames from shot 3.1.3

3.4. After locating the optimal stimulation site, trace a concave line along the anterior edge of the coil and mark the midpoint of this line to indicate the precise hotspot location **[1]**.

3.4.1. Talent tracing a curved line following the anterior coil edge and marking the center point clearly on the patient's cap.

3.5. Now, confirm the identified motor hotspot at regular intervals **[1]**. If refinement is required during a session or treatment cycle, mark the new hotspot on the patient's cap and record the reason for adjustment in the clinical chart **[2]**. To determine the resting motor threshold, begin assessment after allowing the patient a short accommodation period **[3]**.

3.5.1. Talent pointing to the hotspot position during the ongoing session.

3.5.2. Talent marking a new hotspot on the cap and recording notes in the patient's clinical chart.

3.5.3. Talent and patient in position, with the patient resting.

3.6. Deliver transcranial magnetic stimulation pulses at 50 percent of the device's maximum output **[1 and shot 3.5.1 side-by-side]** and confirm that visible muscle contractions of the contralateral hand occur in at least 5 out of 10 pulses **[2]**.

3.6.1. Talent setting the stimulator to 50 percent intensity and applying a series of pulses. **Author's NOTE**: Besides the filmed shot 3.6.1., please add frames from 3.5.1. showing the talent applying a series of pulses. Display 3.6.1 and 3.5.1 together using split screen

Reuse 3.5.1 Talent pointing to the hotspot position during the ongoing session.

3.6.2. Close-up of the patient's hand showing repeated contractions in at least 5 of 10 delivered pulses. **Author's NOTE**: Please use frames from shot 3.1.3

3.7. If visible contractions in at least 5 of 10 pulses are not achieved, increase the stimulation intensity in 2 percent increments until this response criterion is met **[1]**. Once the criterion is achieved, decrease the intensity by 1 percent to identify the minimum level that still elicits a motor response in at least 5 of 10 pulses **[2]**.

3.7.1. SCREEN: Show the device display as the talent increases intensity by 2 percent increments and records response observations. ***Videographer: Please record the device/monitor/screen for the shots labeled as SCREEN***

3.7.2. SCREEN: Show the operator reducing the intensity setting by 1 percent and confirming consistent hand contractions meeting the threshold definition.

3.8. Record the resting motor threshold in the patient's clinical chart for use in upcoming treatment sessions **[1]**. If re-assessment of the resting motor threshold is required, record the new resting motor threshold value along with the reason for re-assessment **[2]**.

3.8.1. Talent writing or typing the resting motor threshold value into the patient's clinical record.

3.8.2. Talent updating the clinical record with a revised resting motor threshold value.

4. Treatment Site (TS) Determination

4.1. After identifying the motor hotspot and determining the resting motor threshold, proceed to locate the treatment site **[1]**. This procedure focuses on non-neuronavigated approaches based on scalp measurements, as these methods are commonly used in clinical practice **[2]**.

4.1.1. Talent pointing to the motor hotspot region.

4.1.2. Talent gathering the tape and other tools for the next step.

4.2. Using the 5-centimeter rule method, extend a parasagittal line anteriorly from the

midpoint of the concave line drawn after determining the motor hotspot **[1]**. Mark the stimulation point for the left dorsolateral prefrontal cortex at a position between 5 and 6 centimeters, most commonly 5.5 centimeters, along this line **[2]**. Then, position the coil on the treatment site **[3]**. **NOTE**: VO added for the extra shot

4.2.1. Talent using a measuring tape to draw an anterior para-sagittal line starting from the midpoint of the previously drawn concave line.

4.2.2. Talent marking a point 5.5 centimeters along this line to indicate the left dorsolateral prefrontal cortex treatment site.

Added shot 4.2.3: Talent positioning the coil on the treatment site

4.3. Alternatively, use the Beam F3 method to locate the F3 position from the 10-20 *(ten-twenty)* electroencephalogram system on the scalp as an alternative landmark for the left dorsolateral prefrontal cortex **[1]**. Input the specific head measurements of the patient into a freely available software that provides instructions for marking F3 according to head size **[2]**.

4.3.1. Talent pointing to the EEG system to identify the position.

4.3.2. SCREEN: Show the software interface where the talent inputs patient head measurements to obtain F3 marking guidance.

4.4. Using a tape, measure the nasion–inion distance from the top of the nose bridge to the bump at the back of the skull **[1]**. Second, measure the intertragus distance from one ear's tragus to the other **[2]**. Third, measure the head circumference by passing the tape over the inion at eyebrow level **[3]**.

4.4.1. Talent measuring the nasion–inion distance across the top of the patient's head using a tape measure.

4.4.2. Talent measuring the intertragus distance by stretching the tape between both tragi.

4.4.3. Talent measuring the head circumference by passing the tape over the inion and above the eyebrows.

4.5. Input the three measurements into the software to generate two output distances **[1]**. The first output, Point X, provides the distance to the left of the midline along the head circumference **[2]**, and the second, gives the distance from the vertex along a line intersecting Point X **[3]**. Use these two distances to mark Point Y on the patient's scalp as the left dorsolateral prefrontal cortex treatment site **[4]**.

4.5.1. Talent recording the measured values for entry into the computer.

4.5.2. SCREEN: Cursor hovering over computed outputs for Point X.

4.5.3. SCREEN: Cursor hovering over computed Point Y based on the input measurements.

4.5.4. Talent marking Point Y on the patient's scalp to indicate the final treatment site.

4.6. Finally, confirm the treatment site at regular intervals. If refinement is necessary, mark the updated treatment site on the patient's cap **[1]** and document the reason for adjustment in the clinical chart, whether by protocol or due to other factors **[2]**.

4.6.1. Talent pointing to the treatment site alignment marking a refined treatment site on the cap.

4.6.2. Talent updating the clinical chart.

Results

5. Results

5.1. A total of 35 treated patients were included in this study of real-world evidence. Mean MADRS *(M-A-D-R-S)* total score decreased significantly after 6 weeks of treatment compared to baseline **[1-TXT]**.

5.1.1. LAB MEDIA: Figure 1A. *Video editor: Highlight the data point "Post Treatment"*
TXT: MADRS: Montgomery-Asberg Depression Rating Scale

5.2. The mean reduction in MADRS was 9.13 points, demonstrating a statistically significant antidepressant effect after the treatment period **[1]**.

5.2.1. LAB MEDIA: Figure 1A. *Video editor: Focus on the horizontal square bracket above with the * sign.*

5.3. Following treatment, 56.7% of patients achieved partial response **[1]**, 46.7% met the criteria for response **[1=2]**, and 43.3% reached remission **[3]**.

5.3.1. LAB MEDIA: Figure 1B. *Video editor: Highlight the bar labelled "Partial Response" with "56.7%"*.

5.3.2. LAB MEDIA: Figure 1B. *Video editor: Highlight the bar labelled "Response" with "46.7%"*.

5.3.3. LAB MEDIA: Figure 1B. *Video editor: Highlight the bar labelled "Remission" with "43.3%".*

- nasion

Pronunciation link: https://www.merriam-webster.com/dictionary/nasion
IPA: /ˈneɪziən/
Phonetic Spelling: nay-zee-uhn

- inion

Pronunciation link: https://www.merriam-webster.com/dictionary/inion
IPA: /ˈɪniən/
Phonetic Spelling: in-ee-uhn

- intertragus

Pronunciation link: No confirmed link found

IPA: /ˌɪntərˈtreɪgəs/
Phonetic Spelling: in-ter-tray-guhs

- parasagittal
Pronunciation link: https://www.merriam-webster.com/dictionary/parasagittal
IPA: /ˌpærəˈsædʒɪtəl/
Phonetic Spelling: par-uh-saj-i-tuhl

- dorsolateral
Pronunciation link: https://www.merriam-webster.com/dictionary/dorsolateral
IPA: /ˌdɔːrsoʊˈlætərəl/
Phonetic Spelling: dor-soh-lat-uh-rul

- lycra
Pronunciation link: https://www.oxfordlearnersdictionaries.com/definition/english/lycratm oxfordlearnersdictionaries.com+2Cambridge Dictionary+2
IPA: /ˈlaɪkrə/
Phonetic Spelling: lie-kruh

- cap (in context "lycra cap") — common word, no special pronunciation needed.

- earplugs — common word, no special pronunciation needed.

- transcranial (as in "transcranial magnetic stimulation")
Pronunciation link: No confirmed link found
IPA: /ˌtrænzˈkreɪniəl/
Phonetic Spelling: tranz-kray-nee-uhl

- magnetic — common word, though some may find the "mag-net-ic" division helpful.
Pronunciation link: https://www.merriam-webster.com/dictionary/magnetic
IPA: /mægˈnɛtɪk/
Phonetic Spelling: mag-net-ik

- stimulation — common word, but for precision: https://www.merriam-webster.com/dictionary/stimulation
IPA: /ˌstɪmjəˈleɪʃən/
Phonetic Spelling: stim-yoo-lay-shun

- motor (in "motor hotspot", "motor cortex") — common word: https://www.merriam-webster.com/dictionary/motor

IPA: /ˈmoʊtər/
Phonetic Spelling: mo-ter

- hotspot (in neuro context) — common composite word; but you could divide “hot-spot”. No special link.

IPA: /ˈhɑtˌspɑt/
Phonetic Spelling: hot-spot

- cortex (in “motor cortex”, “prefrontal cortex”)

Pronunciation link: https://dictionary.cambridge.org/dictionary/english/cortex
IPA: /ˈkɔːrteks/ (US)
Phonetic Spelling: kor-teks

- nasion

Pronunciation link: https://www.merriam-webster.com/dictionary/nasion
IPA: /ˈneɪziən/
Phonetic Spelling: nay-zee-uhn

- inion

Pronunciation link: https://www.merriam-webster.com/dictionary/inion
IPA: /ˈɪniən/
Phonetic Spelling: in-ee-uhn

- intertragus (in “intertragus line”)

Pronunciation link: No confirmed link found
IPA: /ˌɪntərˈtreɪgəs/
Phonetic Spelling: in-ter-tray-guhs

- mid-sagittal (in “mid-sagittal line”)

Pronunciation link: No confirmed link found
IPA: /ˌmɪd səˈdʒɪtəl/
Phonetic Spelling: mid suh-jit-uhl

- parasagittal (in “anterior para-sagittal line”)

Pronunciation link: https://www.merriam-webster.com/dictionary/parasagittal
IPA: /ˌpærəˈsædʒɪtəl/
Phonetic Spelling: par-uh-saj-i-tuhl

- dorsolateral (in “left dorsolateral prefrontal cortex”)

Pronunciation link: https://www.howtopronounce.com/dorsolateral-prefrontal-cortex howtopronounce.com+1
IPA: /ˌdɔːrsoʊˈlætərəl/
Phonetic Spelling: dor-soh-lat-uh-rul

- prefrontal (in “prefrontal cortex”)

Pronunciation link: https://dictionary.cambridge.org/pronunciation/english/prefrontal-cortex Cambridge Dictionary
IPA: /ˌpriːˈfrʌntəl/
Phonetic Spelling: pree-frun-tuhl

- EEG (abbreviation of electroencephalogram)

Pronunciation link: https://dictionary.cambridge.org/pronunciation/english/eeg Cambridge Dictionary
IPA: /ˌiː iːˈdʒiː/ or simply /ˌiːiːˈdʒiː/
Phonetic Spelling: ee-ee-jee

- electroencephalogram (in description of EEG)

Pronunciation link: https://www.howtopronounce.com/electroencephalogram (though I didn’t check directly)
IPA: /ɪˌlɛktroʊˌɛnsəˈfæləˌgræm/
Phonetic Spelling: ih-lek-troh-en-suh-fal-oh-gram

- resting motor threshold (rMT) — “threshold” and “resting” are common words; “threshold” pronunciation: https://www.merriam-webster.com/dictionary/threshold

IPA: /ˈθrɛʃhoʊld/
Phonetic Spelling: thresh-hohld

- Triangle, diagonal, midpoint, etc – common words, no special pronunciation needed for your purposes.

- clinician/clinical (in “clinical chart”, “clinical record”) — common word: https://www.merriam-webster.com/dictionary/clinical

IPA: /ˈklɪnɪkəl/
Phonetic Spelling: klin-i-kuhl

- parasagittal line — we already listed “parasagittal”.

- figure-of-eight coil (common jargon) — “figure-of-eight” is a standard compound; “coil” is common.

- contralateral (in “contralateral hand muscles”)

Pronunciation link: No confirmed link found
IPA: /ˌkɒntrəˈlætərəl/
Phonetic Spelling: kon-truh-lat-uh-rul