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A new device to improve target localization for transcranial magnetic stimulation therapy

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A B S T R A C T

Background: Accurate identification of cranial midline structures is essential for many targeting techniques that use repetitive transcranial magnetic stimulation (rTMS), including the Beam F3 method used for depression treatment.

Objective: Evaluate whether a novel, laser-sighted device will assist with more accurate identification of the cranial midline relative to standard scalp-based measurement procedures.

Methods: Three trained TMS technicians performed repeated scalp-based measurements to identify the inion and vertex on five subjects (n = 54 measurements). Measurements were compared to points identified with the midline localizer device and the true midline as defined by MRI midline structures.

Results: Use of the midline localizer was more accurate for midline identification than technician measurement ($p = 0.00025$) and the ratio of localizing the midline within 5 mm was higher (78% versus 54%, $p = 0.008$).

Conclusion: Use of a laser-sighted midline localizer device can improve the accuracy of scalp measurements associated with target localization for rTMS treatment protocols.

Dear editor:

Repetitive transcranial magnetic stimulation (TMS) is an FDA-approved treatment for major depressive disorder when targeted at the left prefrontal cortex [1]. However, the optimal cortical target within the left prefrontal cortex and the ideal method for identifying the target are unclear [2–4]. One of the most commonly used targeting methods, Beam F3, utilizes scalp landmarks to identify a left prefrontal brain region that corresponds with the F3 location of a 10–20 EEG measurement system [5]. The reliability of target identification with Beam F3 requires accurate identification of the cranial midline at the inion of the skull and the cranial vertex. To date, little research exists to examine the reliability and reproducibility of identification of these cranial midline targets, though the introduction of any error in these measurements would compromise successful target localization. Here we aim to test whether a novel laser-sighted device is capable of improving midline localization by quickly and efficiently minimizing measurement error relative to standard scalp-based measurement procedures.

We designed a horseshoe-shaped device, termed the “cranial midline localizer,” or more colloquially, the “wishbone.” It is adjustable to head size, with “calipers” that anchor in the bilateral external auditory canals with metallic spheres (Fig. 1A). A laser sight is located at the top of the device with a sighting mechanism to ensure the laser consistently illuminates the midpoint between the two metallic spheres. The device can swivel around its anchor point in the auditory canals, allowing identification of midline targets at any point along the mid-sagittal plane. For the purposes of this study, the device was used to plot points at the midline vertex and inion/occiput of the head (see supplementary online video).

Five healthy young subjects, four male, ages of 29–44 (mean 35.4) were recruited for the study. A second replication sample was obtained (measurements by 3 technicians across 7 subjects, four male, ages 20–44; mean 31.9). The study was approved by the University of Iowa Institutional Review Board and all subjects signed consent.

A T1-weighted structural MRI was obtained on a 7T GE MR950 scanner within 30 days of participation. Images were resampled to 1 mm isotropic voxels and the intensity range was truncated to standardize values from air-to-scalp-to-skull. The processed images were loaded into Brainsight neuronavigation equipment (Rogue Research, Montreal, Quebec) for measurement.

Three trained TMS technicians performed repeated scalp measurements on each of the 5 subjects at various time points over the course of one month (n = 54 measurements, 27 at each of two targets; 6 to 18 measurements per subject). Two targets were investigated: 1) the vertex compared to the falx cerebri midline on MRI, and 2) the inion/midline occiput compared to an MRI-defined midline occiput. This MRI occiput was identified by a posterior point in the mid-sagittal plane that bisected the falx cerebri, third ventricle, and cerebral aqueduct. A second sample including only vertex measurements was also analyzed (3 technicians x 3 time points = 9 measurements per subject x 7 subjects = 63 measurements − 1 lost data point = 62 measurements). Technicians used visual inspection, palpation of scalp landmarks, and tape

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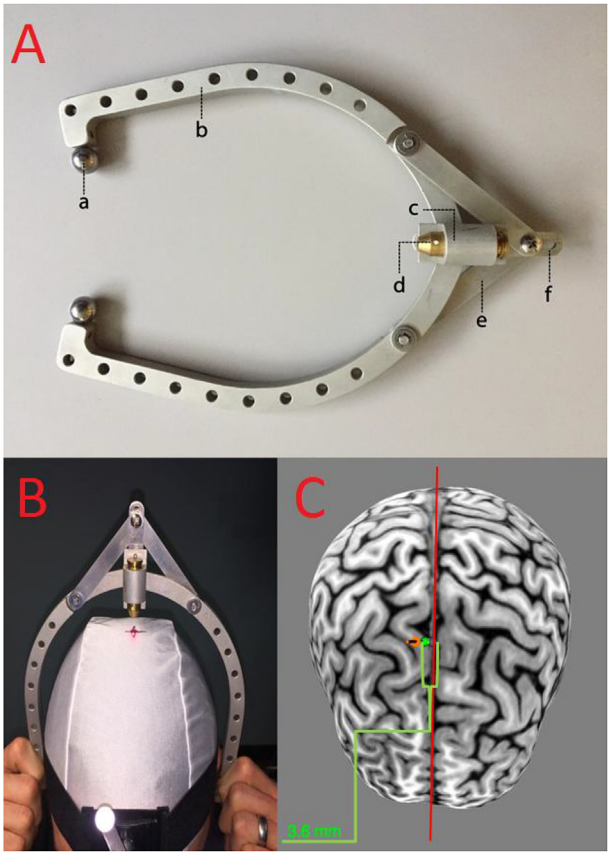

Fig. 1. **(A)** The "wishbone" and its components: **a)** External auditory canal sphere; **b)** caliper arm; **c)** laser pointer dock; **d)** laser pointer; **e)** sliding caliper adjustment arm; **f)** midline sighting housing. The device anchors in the external auditory canals of the patient. The laser pointer sits dorsally for vertex measurements and posteriorly for midline occiput measurements. **(B)** Example of technician-identified vertex target (black cross) matching up with "wishbone" laser pointer midline (red dot). **(C)** Technician or "wishbone"-identified midline target is plotted on Brainsight 3D brain reconstruction and software used to calculate distance from estimated midline (orange pin inserting into green sphere) to true midline of falx cerebri (red line). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

measurement according to standard clinical practices to identify the two midline targets in each subject, as required for Beam F3 targeting (clinicalresearcher.org) [5]. The midline landmarks were marked on a Lycra cap worn by the subject and immediately plotted onto the patient's brain MRI using Brainsight. Technician measurements were compared to the midline identified by the "wishbone" device, and both were compared to a "gold standard" MRI-defined midline (Fig. 1B and C). The two main analyses focused on 1) whether the "wishbone" resulted in less distance from the midline compared to technician measurements, evaluated using a T-test, and 2) whether there was a higher proportion of measurements within a predefined 5 mm margin of error using the "wishbone," evaluated with a Chi-square test. Standard figure-8 TMS coils are thought to stimulate a brain region on the order of 1–2 cm^2 [6], so cumulative error > 5 mm was selected as a threshold for stimulating unwanted or unexpected brain structures.

Across all recorded measurements the wishbone was significantly more accurate in identifying the midline compared to technician-based measurements ($n = 54$; 2.94 ± 2.64 mm versus 5.34 ± 4.74 mm, $p = 0.00025$). This difference was significant when analyzing results from the vertex or inion independently (see online Supplemental Table 1, $p = 0.003$ and $p = 0.008$, respectively). The wishbone outperformed the technician measurements with 78% accuracy within 5 mm of the actual midline compared to 54% for technician measurements ($p = 0.008$, chi square) - see Supplemental Table 2 for details, along with proportional accuracy as defined by 1 mm or 10 mm. Notably, use of the wishbone to confirm or correct midline vertex and occiput targets added less than 15 seconds of technician time per patient and would have resulted in >5 mm corrections of technician targeting 20% of the time (including 37% of inion measurements).

This data highlights the challenges with reliable target identification by TMS technicians utilizing the Beam F3 method. The vertex and inion are especially critical landmarks that serve as guidepoints for later measurements (e.g. nasion-to-inion distance) and directly impact the accuracy of the final stimulation site. While no evidence to date confirms that more precise or reliable targeting of TMS therapy results in better outcomes for patients [7], it remains important to know where one is stimulating, and to reliably stimulate the target intended by the targeting method to enable valid scientific inquiry and further optimization of treatment parameters. The data in this report demonstrates that use of a laser-sighted midline localizer device, nicknamed the "wishbone," efficiently identifies the scalp midline at the vertex and inion with a greater degree of accuracy than technician-identified landmarks. As such, one could envision the "wishbone" device incorporated into the Beam F3 targeting procedure as a quality control measure that minimizes error in identifying midline structures. This will help ensure the successful identification of a reliable and valid F3 target for repetitive TMS treatment protocols for depression therapy.

Conflicts of Interest/Financial Disclosure

The University of Iowa has filed a provisional patent application for the Wishbone device. Drs. Zanaty, Holland, and Howard are listed as inventors. There are no other financial disclosures or conflicts of interest to report for any of the authors.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brs.2019.07.028.

References

[1] Perera T, et al. The clinical TMS society consensus Review and treatment recommendations for TMS therapy for major depressive disorder. Brain Stimul 2016;9(3):336–46.
[2] Fox MD, Liu H, Pascual-Leone A. Identification of reproducible individualized targets for treatment of depression with TMS based on intrinsic connectivity. Neuroimage 2013;66:151–60.
[3] Mir-Moghtadaei A, et al. Concordance between BeamF3 and MRI-neuronavigated target sites for repetitive transcranial magnetic stimulation of the left dorsolateral prefrontal cortex. Brain Stimul 2015;8(5):965–73.
[4] Johnson KA, et al. Prefrontal rTMS for treating depression: location and intensity results from the OPT-TMS multi-site clinical trial. Brain Stimul 2013;6(2):108–17.
[5] Beam W, et al. An efficient and accurate new method for locating the F3 position for prefrontal TMS applications. Brain Stimul 2009;2(1):50–4.
[6] Deng ZD, Lisanby SH, Peterchev AV. Electric field depth-focality tradeoff in transcranial magnetic stimulation: simulation comparison of 50 coil designs. Brain Stimul 2013;6(1):1–13.
[7] Levkovitz Y, et al. Efficacy and safety of deep transcranial magnetic stimulation for major depression: a prospective multicenter randomized controlled trial. World Psychiatry 2015;14(1):64–73.

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