Brain Stimulation 15 (2022) 1465–1466

Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: http://www.journals.elsevier.com/brain-stimulation

Comparison of consistency between image guided and craniometric transcranial magnetic stimulation coil placement

Traditionally, rTMS treatment of the DLFPC has been located using craniometric strategies; manual methods of scalp measurement used to help identify the appropriate location to place the coil for stimulating the underlying brain [1]. Examples of such craniometric approaches include the "5-cm rule" [1,2] and more recently, the "Beam-F3'' strategy, which were initially designed to attempt to stimulate the Left DLPFC [1,3]. These approaches to craniometric targeting are widely used in the field, and the principal reason given for their use over image guidance-based approaches is based on cost considerations, as using image guidance requires the purchase of additional equipment [2]. Unfortunately, both methods have demonstrated variability and often miss the ideal target location partially or completely [4,5].

In this study, we systematically tested whether craniometric targeting methods were similarly poor at reproducibly treating the same part of the brain when compared to an image-guided method using a personalized brain map derived through machine learning. Specifically, we had experienced rTMS treatment technicians perform three different approaches to placing the TMS coil and tested the between-technician variation in where they were placing the coil with each approach.

We had 12 healthy adult subjects undergo MRI brain imaging, including T1 MP-Rage and diffusion tractography imaging. The imaging data was processed and the creation of a personalized brain map using machine learning-derived parcels was used using the methods described previously by our group [6]. Each subject's T1 was co-registered with overlay objects for left and right Brodmann area 46 within the DLPFC, exported to the Localite neuronavigation system (Bonn, Germany). The optimal coil placement location was automatically generated in Localite by highlighting the centroid of the area 46 parcel and selecting the "Calculate Entry" option. This provides an entry point based on the shortest distance to the skull. Each method (the 5-cm rule, Beam-F3 and image-guided) was performed by three experienced TMS technicians with the craniometric approaches being performed using a soft ruler as per the standard use. Each method was performed as an independent event to the others, in a random order, and the Talairach coordinate for each approach was recorded when the technician stated that they were at the intended target. Additionally, due to the innate difficulty to blind technicians from the condition, we attempted to minimize this effect by placing the coil on both hemispheres of the head to reduce the risk of a technician position or handedness biasing one approach or another.

It was found that targeting Brodmann area 46 using the image-guided approach substantially decreased the variability in target location compared to either craniometric approaches on the left side (Image-guided vs 5-cm vs Beam-F3, $p < .001$) and right side (Image-guided vs 5-cm vs Beam-F3, $p < .001$). The image-guided approach has greater accuracy in locating area 46 compared to the craniometric methods (Fig. 1). To determine the biologic relevance of this finding, an analysis of the intended parcel of stimulation (target location) was undergone to reveal the expected large scale brain network that would likely be centered under the coil. Target parcel accuracy is as follows; left: 95%, 58%, and 33%; right: 89%, 33%, and 31% for neuronavigated, 5cm, and Beam-F3, respectively. For neuronavigated, parcel network mapping included the Central Executive and Multiple Demand networks. For both the 5-cm rule and Beam-F3, parcel network mapping included the Central Executive, Ventral Attention, Salience, Sensorimotor, Language and Multiple Demand Networks.

While the best location in the cerebral cortex to direct rTMS therapy is still a matter of active study, it would likely follow that administering treatments with inconsistent target locations between sessions may be inferior to administering precise and consistent treatments at every session. It would be assumed that even if it's the suboptimal location to stimulate, we could draw stronger inferences about that location's efficacy at improving a patient's symptoms if the treatment is stimulating a consistent area of cortex.The current study provides evidence that the use of craniometric methods to target rTMS treatment in the DLPFC leads to substantially reduced reproducibility compared to the use of image guidance-based targeting techniques combined with a personalized brain map [6]. Despite the presence of experienced TMS technicians, craniometric targeting techniques displayed increased variance for finding the DLPFC by nearly 7-fold. Thus, it is implausible that the treatment is being centered over the same area every treatment session, even with experienced technicians.

While it is intuitive that using a computer-based guidance system is a superior approach to using a tape measure to locate the treatment site on the scalp, it is difficult to prove this in a definitive way [7,8]. Principally, this is because treatment outcomes following rTMS treatment for major depression are dependent on numerous factors other than the method of targeting [7,9]. Thus, a successful or failed clinical trial can be potentially explainable by factors other than the independent variable being randomized, especially given the relatively modest sample size of most rTMS trials, which are generally too small to randomize away the effect of some highly heterogeneous confounders [1,3]. Especially given there are so many sources of potential error during craniometric coil placement, such as, but not limited to, heterogenous skull and cortical anatomy, significant variations in soft ruler measurements of the cranium in one individual both between different technicians and

https://doi.org/10.1016/j.brs.2022.10.008

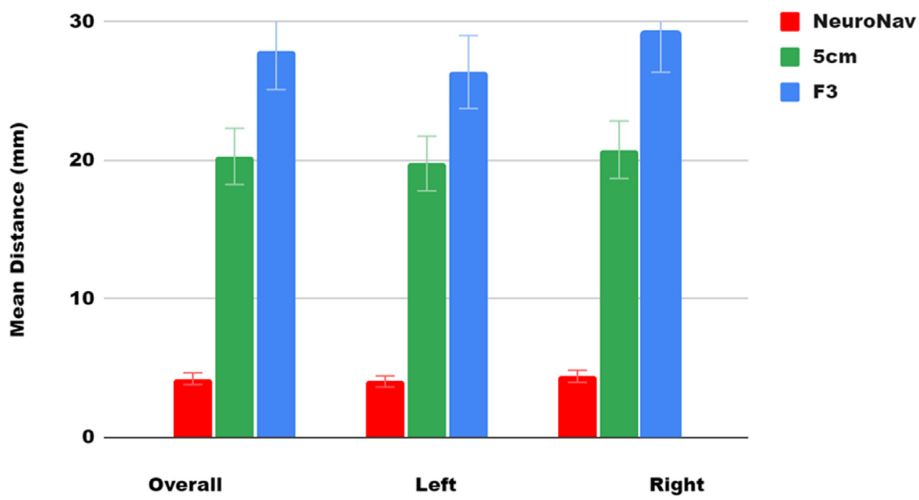

Fig. 1. Target Variance with different TMS positioning methods.
Three technicians placed the transcranial magnetic stimulation coil on each hemisphere of a participant's head using three coil placement methods. Two of these methods were craniometric: the "5-cm rule" and Beam-F3; the other was using neuronavigation guided at the subjects' Brodmann area 46. The Talairach coordinate for the ideal coil placement location was defined based on the shortest distance to the skull from Brodmann area 46. Following the technician placing the coil, the Talairach coordinate of its placement was noted for each method and hemisphere. These coordinates were then used to calculate the distance from the ideal coil placement location using the Euclidean formula. The 'Overall' columns represent the average variance of coil positioning from the ideal coil placement from both the left and right measurements of all subjects. This demonstrates that the Neuronavigation method had significantly less variance overall and for both the left and right hemispheres. Additionally, the 5cm rule had the second smallest variance, whereas the Beam F3 had the greatest variance from the target. Definitions: Mm = millimeters, NeuroNav = neuronavigation method, 5cm = 5cm rule, F3 = Beam F3.

the same technician, and technician-related variables including height and personal method of using the craniometric technique.

This study demonstrates the superiority of image-guidance based methods of TMS coil placement, utilizing a personalized brain atlas to determine the treatment location. Craniometric methods have a long-standing history, despite inherent inaccuracy due to a lack of consistent practice. For patients to receive the best care, medical practitioners need to be following the best evidence-based practice and from this study, image-guidance based methods are the way forward. Treating treatment resistant major depression with TMS has great potential, but to fulfill said potential, TMS methodology needs to be refined and optimized with technologies that offer personalized brain maps, especially considering the many confounding factors that can already limit TMS effectiveness. Therefore, it is integral that image-guidance based methods for TMS coil positioning are adopted as the gold standard to maximize treatment outcomes for patients with treatment resistant major depression.

Declaration of competing interest

Some authors (IY, OT, KO, HT, PN, OC, AM, SD, and MS) are employees of Omniscient Neurotechnology.

References

[1] Fitzgerald PB. Targeting repetitive transcranial magnetic stimulation in depression: do we really know what we are stimulating and how best to do it? Brain Stimul 2021;14(3):730–6.
[2] McClintock SM, Reti IM, Carpenter LL, et al. Consensus recommendations for the clinical application of repetitive transcranial magnetic stimulation (rTMS) in the treatment of depression. J Clin Psychiatr 2018;79(1).
[3] Trapp NT, Bruss J, King Johnson M, et al. Reliability of targeting methods in TMS for depression: Beam F3 vs. 5.5 cm. Brain Stimul 2020;13(3):578–81.
[4] Fox MD, Buckner RL, White MP, Greicius MD, Pascual-Leone A. Efficacy of transcranial magnetic stimulation targets for depression is related to intrinsic functional connectivity with the subgenual cingulate. Biol Psychiatr 2012 Oct 1;72(7):595–603. https://doi.org/10.1016/j.biopsych.2012.04.028. Epub 2012 Jun 1. PMID: 22658708; PMCID: PMC4120275.
[5] Cardenas VA, Bhat JV, Horwege AM, et al. Anatomical and fMRI-network comparison of multiple DLPFC targeting strategies for repetitive transcranial magnetic stimulation treatment of depression. Brain Stimul 2022;15(1):63–72.
[6] Doyen S, Nicholas P, Poologaindran A, et al. Connectivity-based parcellation of normal and anatomically distorted human cerebral cortex. Hum Brain Mapp 2022;43(4):1358–69.
[7] Hebel T, Göllnitz A, Schoisswohl S, et al. A direct comparison of neuronavigated and non-neuronavigated intermittent theta burst stimulation in the treatment of depression. Brain Stimul 2021;14(2):335–43.
[8] Rusjan PM, Barr MS, Farzan F, et al. Optimal transcranial magnetic stimulation coil placement for targeting the dorsolateral prefrontal cortex using novel magnetic resonance image-guided neuronavigation. Hum Brain Mapp 2010;31(11):1643–52.
[9] Fitzgerald P. Is it time to introduce repetitive transcranial magnetic stimulation into standard clinical practice for the treatment of depressive disorders? Aust N Z J Psychiatr 2003;37(1):5–11. ; discussion 2-4.

Isabella M. Young, Karol Osipowicz, Alana Mackenzie, Oliver Clarke, Hugh Taylor, Peter Nicholas
Omniscient Neurotechnology, Sydney, 2000, Australia

Mark Ryan, Jonas Holle
Cingulum Health, Rosebery, 2018, Australia

Onur Tanglay, Stephane Doyen
Omniscient Neurotechnology, Sydney, 2000, Australia

Michael E. Sughrue*
Omniscient Neurotechnology, Sydney, 2000, Australia

Cingulum Health, Rosebery, 2018, Australia

* Corresponding author. Omniscient Neurotechnology, Level 10, 580 George St Sydney, NSW, Australia.
E-mail address: sughruevs@gmail.com (M.E. Sughrue).

28 July 2022
Available online 26 October 2022