Brain Stimulation 15 (2022) 1063–1064

Contents lists available at ScienceDirect

Brain Stimulation

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

The therapeutic potential of personalized connectivity-guided transcranial magnetic stimulation target over group-average target for depression

Dear Editor,

Repetitive transcranial magnetic stimulation (rTMS) has been widely used to treat the major depressive disorder (MDD) with a common target over the left dorsolateral prefrontal cortex (DLPFC) [1]. Studies have shown that the left DLPFC targets with better antidepressant efficacy were more negatively correlated with the subgenual cingulate cortex (sgACC), suggesting rTMS efficacy might be improved via functional connectivity (FC)-guided targeting [2–4]. A multi-site rTMS study using the group-average DLPFC target, defined as the most negative FC with sgACC from a cohort of healthy controls, reported a high response rate of 49% in MDD [5]. Establishing a group-level DLPFC target has the advantages of being robust and minimizing noise effects but ignoring the individual variability in sgACC-DLPFC functional connectivity [6]. Some studies have proposed that the personalized DLPFC targets, defined as the individual maximal sgACC-DLPFC functional connectivity, may bring a better efficacy than the group-average DLPFC target [6,7]. Stanford Neuromodulation Therapy demonstrated a high remission rate of 79% by using personalized DLPFC targets and an accelerated, high-dose protocol [8]. However, whether rTMS with personalized DLPFC targets has the therapeutic advantage over the group-average target for depression remains unclear in the lack of direct comparisons between antidepressant outcomes from these two targeting methods.

Two retrospective studies provided an alternative way to examine the therapeutic potential of personalized DLFPC targets relative to other targeting methods [9,10]. By calculating the Euclidean distances between the actual targets from the 'Beam F3′ method [9] and the '5.5 cm' method [10] and personalized DLPFC targets, they found a better antidepressant outcome with a closer distance to the personalized target, suggesting the therapeutic potential of personalized DLPFC targets relative to the two conventional targeting methods. In our MDD patients who received rTMS previously over the group-average DLPFC site, we followed the same logic to investigate the therapeutic potential of personalized DLPFC targets relative to the group-average target. We hypothesized that closer proximity between group-average and personalized targets would be associated with better antidepressant outcomes.

The present study recruited 18 MDD outpatients between January 2018 and March 2021 at Shanghai Mental health Center (SHMC). The institutional ethical board of SMHC approved the protocol (2017–43), and all participants provided written consent before study entry. They all received 10-Hz rTMS treatment every weekday, amounting to 20 sessions. A common precise DLPFC target (Montreal Neurological Space coordinates: −42, 44, 30) was used with a group-average maximal sgACC-DLPFC connectivity [3]. The target was localized using individual structural MRI data guided by the Localite Neuronavigation System (NDI, Canada). All patients completed the Montgomery-Asberg Depression Rating Scale (MADRS) assessments, structural magnetic resonance imaging (MRI), and resting-state functional MRI acquisitions before and after 20-session rTMS treatment. MRI data were collected from a 3.0 T Siemens Verio MRI scanner (MRB17, Siemens AG, Erlangen, Germany) in SMHC (detailed parameters in supplementary

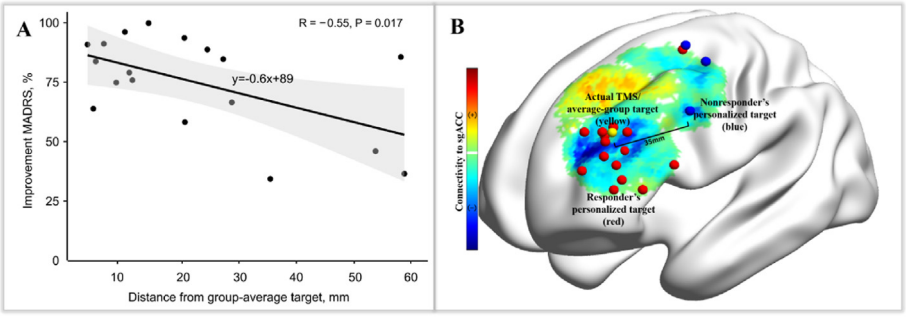

Fig. 1. (A) Closer proximity between the group-average target and personalized target was associated with improved treatment response. (B) Patients (N = 18) received the rTMS treatment over the common group-average target (yellow dot). Personalized sgACC-DLPFC targets were retrospectively computed and depicted by the red dots (responders) or the blue dots (nonresponders). MADRS, Montgomery-Asberg Depression Rating Scale; sgACC, the subgenual cingulate cortex; DLPFC, the dorsolateral prefrontal cortex. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

https://doi.org/10.1016/j.brs.2022.07.054

materials). Functional connectivity was computed between each voxel within the left DLFPC and a sgACC-based seed map which substituted sgACC to improve the signal-to-noise ratio [6]. The personalized DLPFC target was identified by the sphere's center with a radius of 9 mm with a maximum of negative FC values. The Euclidean distance between group-average DLPFC target and personalized DLPFC targets was calculated, while the correlation of the distance and percentage improvement in MARDS score by rTMS was examined.

Of 18 MDD patients, 11 (61%) were female, the mean (SD) age was 31 (6) years old. The mean (SD) percentage of improvements in MARDS score was 75% (20%). Closer proximity between the group-average and personalized targets was significantly correlated with better MADRS improvements ($R = -0.554$; $P = 0.017$) (Fig. 1A). According to the fitted line, the mean percentage of improvement in MARDS score would be 89% if all depressive patients received rTMS over personalized targets (Fig. 1A). Compared to the actual group-average target, target site personalization further took a 14% increase in MADRS improvements theoretically. The response rate was 100% ($n = 14$ of 14) for patients when the distance to the group-average target was closer than 29 mm. The response rate was 25% ($n = 1$ of 4) for the remaining patients whose personalized targets were far away from the group-average target (Fig. 1B).

In general, MDD patients showed better antidepressant improvements when the actual group-average target was closer to the personalized target. Our results suggested that target site personalization indicates a degree of potential therapeutic benefits for MDD even over the group-average target. Limitations of the present study include the retrospective evaluation and moderate sample size.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

This work was supported by National Nature Science Foundation of China (81871050, 81971251); Natural Science Foundation of Shanghai (17ZR1424700, 21ZR1481500); Key Projects of Shanghai Clinical Research Center (CRC2018ZD01, CRC2019ZD02); Shanghai Clinical Research Center for Mental Health (19MC1911100); Project of the Key Discipline Construction, Shanghai 3-Year Public Health Action Plan (GWV-10.1-XK18). Yingying Tang is funded by Shanghai Municipal Education Commission— Gaofeng Clinical Medicine Grant Support (20191836).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brs.2022.07.054.

References

[1] Jean-Pascal L, André A, Chris B, H BD, Jérôme B, Vincenzo DL, et al. Corrigendum to “Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS): an update (2014-2018). Clin Neurophysiol 2020;131:474–528. https://doi.org/10.1016/j.clinph.2020.02.003.

[2] 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;72:595–603. https://doi.org/10.1016/j.biopsych.2012.04.028.

[3] Weigand A, Horn A, Caballero R, Cooke D, Stern AP, Taylor SF, et al. Prospective validation that subgenual connectivity predicts antidepressant efficacy of transcranial magnetic stimulation sites. Biol Psychiatr 2018;84:28–37. https://doi.org/10.1016/j.biopsych.2017.10.028.

[4] Cash RFH, Zalesky A, Thomson RH, Tian Y, Cocchi L, Fitzgerald PB. Subgenual functional connectivity predicts antidepressant treatment response to transcranial magnetic stimulation: independent validation and evaluation of personalization. Biol Psychiatr 2019;86:e5–7. https://doi.org/10.1016/j.biopsych.2018.12.002.

[5] Blumberger DM, Vila-Rodriguez F, Thorpe KE, Feffer K, Noda Y, Giacobbe P, et al. Effectiveness of theta burst versus high-frequency repetitive transcranial magnetic stimulation in patients with depression (THREE-D): a randomised non-inferiority trial. Lancet 2018;391:1683–92. https://doi.org/10.1016/s0140-6736(18)30295-2.

[6] 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. https://doi.org/10.1016/j.neuroimage.2012.10.082.

[7] Cash RFH, Cocchi L, Lv J, Wu Y, Fitzgerald PB, Zalesky A. Personalized connectivity-guided DLPFC-TMS for depression: advancing computational feasibility, precision and reproducibility. Hum Brain Mapp 2021;42:4155–72. https://doi.org/10.1002/hbm.25330.

[8] Cole EJ, Phillips AL, Bentzley BS, Stimpson KH, Nejad R, Barmak F, et al. Stanford neuromodulation Therapy (snt): a double-blind randomized controlled trial. Am J Psychiatr 2022;179(2):132–41. https://doi.org/10.1176/appi.ajp.2021.20101429.

[9] Cash RFH, Cocchi L, Lv J, Fitzgerald PB, Zalesky A. Functional magnetic resonance imaging–guided personalization of transcranial magnetic stimulation treatment for depression. JAMA Psychiatry 2021;78(3):337–9. https://doi.org/10.1001/jamapsychiatry.2020.3794.

[10] Siddiqi SH, Weigand A, Pascual-Leone A, Fox MD. Identification of personalized transcranial magnetic stimulation targets based on subgenual cingulate connectivity: an independent replication. Biol Psychiatr 2021;90(10):e55–6. https://doi.org/10.1016/j.biopsych.2021.02.015.

Gai Kong
Shanghai Key Laboratory of Psychotic Disorders, Shanghai Mental Health Center, Shanghai Jiaotong University School of Medicine, Shanghai, 200030, China

Lijiang Wei
Beijing Normal University, State Key Laboratory of Cognitive Neuroscience and Learning, Beijing, China

Jijun Wang
Shanghai Key Laboratory of Psychotic Disorders, Shanghai Mental Health Center, Shanghai Jiaotong University School of Medicine, Shanghai, 200030, China

CAS Center for Excellence in Brain Science and Intelligence Technology (CEBSIT), Chinese Academy of Science, PR China

Bio-X Institutes, Key Laboratory for the Genetics of Developmental and Neuropsychiatric Disorders (Ministry of Education), Shanghai, PR China

Chaozhe Zhu**
Beijing Normal University, State Key Laboratory of Cognitive Neuroscience and Learning, Beijing, China

Yingying Tang*
Shanghai Key Laboratory of Psychotic Disorders, Shanghai Mental Health Center, Shanghai Jiaotong University School of Medicine, Shanghai, 200030, China

** Corresponding author. Beijing Normal University, State Key Laboratory of Cognitive Neuroscience and Learning, Beijing, China.

* Corresponding author. Shanghai Key Laboratory of Psychotic Disorders, Shanghai Mental Health Center, Shanghai Jiaotong University School of Medicine, Shanghai, 200030, China.
E-mail address: czzhu@bnu.edu.cn (C. Zhu).
E-mail address: yytang@smhc.org.cn (Y. Tang).

27 June 2022
Available online 2 August 2022