


Comparison of effectiveness of common targeting heuristics in repetitive transcranial magnetic stimulation treatment of depression

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ABSTRACT

Background Repetitive transcranial magnetic stimulation (rTMS) of the left dorsolateral prefrontal cortex (DLPFC) is an effective non-pharmacological, non-invasive intervention for depression. However, the optimal strategy for localising the DLPFC treatment site on the patient's scalp is heavily disputed. Routine strategies were previously incrementally refined and compared in terms of anatomical accuracy, but little is known about their impact on clinical outcomes.

Objective To assess the impact of three common scalp-based heuristics for magnetic coil positioning on the treatment outcome of rTMS.

Methods This retrospective analysis of real-world clinical data involved patients suffering from a major depressive episode (n=94) who received a 4-week course of excitatory rTMS to the left DLPFC. The treatment target (ie, coil position) was either determined at an absolute distance anterior to the motor hotspot ('6 cm rule') or defined in reference to the EEG electrode position F3 using a traditional ('Beam F3') or optimised ('Beam F3 Adjusted') approach.

Findings There was no statistically significant difference between the '6 cm rule' and the 'Beam F3' method nor between the 'Beam F3' and the 'Beam F3 Adjusted' method in head-to-head comparisons of averaged per cent change of scores on depression rating scales (all p>0.605) and response rate (all p>0.475).

Conclusions Enhancing targeting precision via scalp-based heuristics does not affect treatment outcomes.

Clinical implications There is no need for clinicians to switch from their familiar to an 'advanced' approach among these common targeting heuristics.

INTRODUCTION

High-frequency repetitive transcranial magnetic stimulation (rTMS) of the left dorsolateral prefrontal cortex (DLPFC) is an effective intervention for the treatment of depression.¹ However, where to place the TMS coil on the patient's scalp in order to target the optimal location within the DLPFC is heavily disputed. In clinical practice, most TMS coil positioning approaches use scalp-based heuristics for localising the DLPFC depression target. These include the '5 cm rule', '5.5 cm rule' and '6 cm rule', determining the treatment target at an absolute distance anterior to the cortical hand 'motor hotspot'. Also, the 'Beam F3' and 'adjusted

Beam F3' methods are commonly applied, defining the target in reference to the EEG electrode position F3.^{2–4} While these methods were incrementally refined and compared in terms of anatomical accuracy,⁵ little is known about their impact on clinical outcomes. A recent head-to-head comparison between the '5.5 cm' and the 'Beam F3' targeting methods failed to find clinical efficacy differences in rTMS treatment of depression.⁶ Here, we use real-world clinical data to retrospectively assess whether the 'Beam F3' method is superior to the '6 cm rule' and if the 'adjusted Beam F3' is an enhancement of the original 'Beam F3' method in terms of clinical outcome.

METHODS

Sample 1 comprised 46 patients who were treated at RWTH Aachen University Hospital. Sample 2 comprised 48 patients who were treated at LVR-Klinik Düren (sample size estimations and characteristics in online supplemental file 1). Eligibility for inclusion in the analysis required a primary psychiatric diagnosis of moderate or severe major or bipolar depression according to ICD-10. Patients remained on prescribed medications; adjustments were made as clinically indicated throughout the treatment course.⁶ Excitatory rTMS was applied over the left DLPFC in 20 sessions/4 weeks (online supplemental file 1). Patients were blind to the localisation method (sample 1: 'Beam F3' n=23, 'Beam F3 Adjusted' n=23; sample 2: 'Beam F3' n=24, '6 cm rule' n=24).

Depression severity was assessed using the self-report Beck Depression Inventory revised (BDI-II) as well as the clinician-administered Hamilton Depression Rating Scale (HAM-D-17) in sample 1 and the Beck Depression Inventory (BDI) in sample 2. Treatment primary outcome was operationalised by calculating the per cent change of depression scores from baseline to end of intervention. 'Response' was defined as a sum score reduction of ≥50% from baseline to the end of treatment (statistical procedures in online supplemental file 1).

RESULTS

There was no difference between 'Beam F3' and 'Beam F3 Adjusted' in head-to-head comparisons of averaged per cent change of depression scores in sample 1 (BDI-II: -19.0 ± 7.0 vs -18.8 ± 8.8

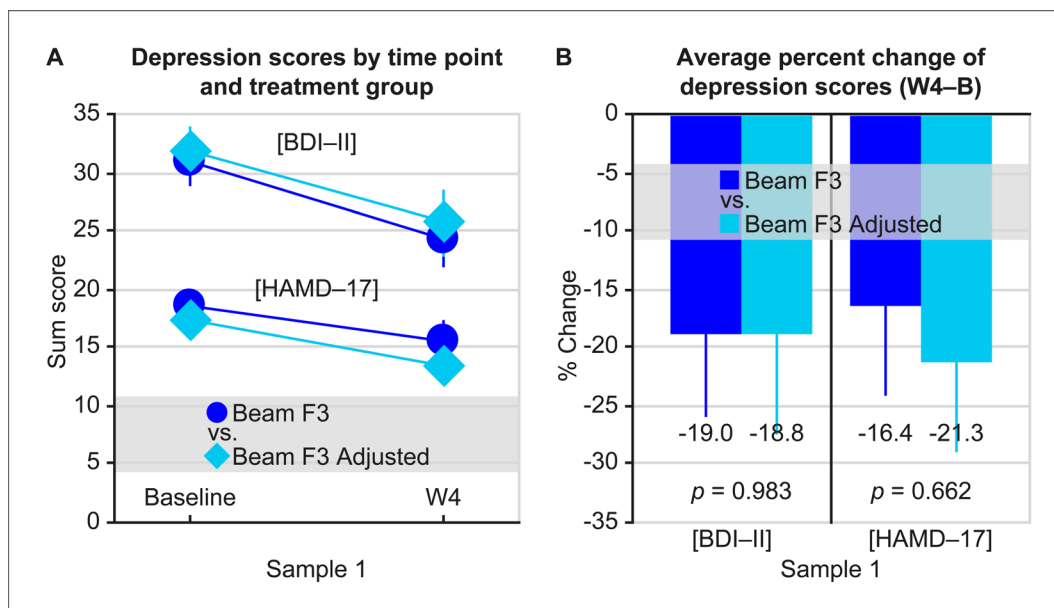


Figure 1 Treatment outcomes of localisation methods ‘Beam F3’ vs ‘Beam F3 Adjusted’ in sample 1 (Aachen). There was neither an interaction between ‘localisation method’ and ‘timepoint’ on depression scores (A) nor a difference in change of depression severity between the localisation methods (B). The main effect was highly significant for the factor ‘timepoint’ (BDI-II: $F_{1,44}=14.151$, $p<0.001$, $\eta^2_p=0.243$; HAMD-17: $F_{1,44}=14.726$, $p<0.001$, $\eta^2_p=0.251$), indicating that depression severity improved during treatment. Mean and SE of the mean are displayed. B, Baseline; BDI-II, Beck Depression Inventory revised; HAMD-17, Hamilton Depression Rating Scale; W4, after week 4/20 sessions of treatment.

($M\pm SEM$), $t_{44}=-0.021$, $p=0.983$, $d_z=-0.006$; HAMD-17: -16.4 ± 7.7 vs -21.3 ± 7.9 ($M\pm SEM$), $t_{44}=-0.440$, $p=0.662$, $d_z=0.130$; **figure 1**). The 2×2 ANOVA indicated no interaction between ‘localisation method’ and ‘timepoint’ (BDI-II: $F_{1,44}=0.016$, $p=0.901$, $\eta^2_p=0.000$; HAMD-17: $F_{1,44}=0.205$, $p=0.653$, $\eta^2_p=0.005$). Response rates were equally distributed (to non-response rates) across the ‘Beam F3’ and ‘Beam F3 Adjusted’ localisation methods (BDI-II: 26.1 vs 17.4 (%), $\chi^2_1=0.511$, $p=0.475$, $\varphi=0.105$; HAMD-17: 13.0 vs 13.0 (%), $\chi^2_1=0.000$, $p=1.000$, $\varphi=0.000$) (further details in online supplemental file 1).

There was also no difference between ‘Beam F3’ and the ‘6 cm rule’ in head-to-head comparisons of averaged per cent change of depression scores in sample 2 (BDI: -25.7 ± 6.0 vs -29.9 ± 5.1 ($M\pm SEM$), $t_{46}=0.520$, $p=0.605$, $d_z=0.150$; **figure 2**). Also here, the 2×2 ANOVA indicated no interaction between ‘localisation method’ and ‘timepoint’ ($F_{1,46}=0.579$, $p=0.450$, $\eta^2_p=0.012$). Also across the ‘Beam F3’ and ‘6 cm rule’ localisation methods,

(further details in online supplemental file 1).

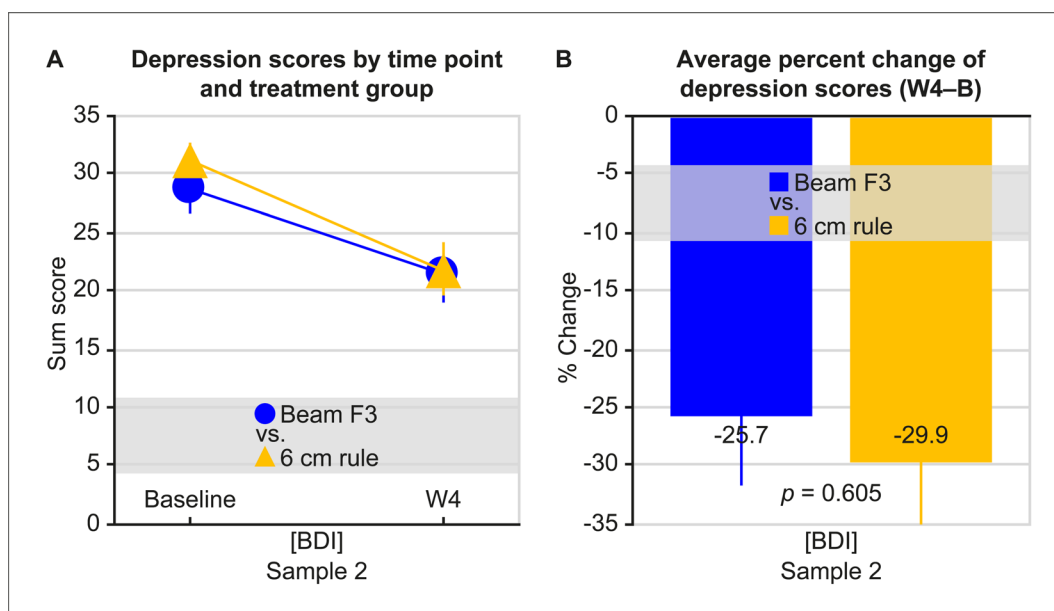


Figure 2 Treatment outcomes of localisation methods ‘Beam F3’ vs ‘6 cm rule’ in sample 2 (Düren). There was neither an interaction between ‘localisation method’ and ‘timepoint’ on depression scores (A) nor a difference in change of depression severity between the localisation methods (B). There was a highly significant main effect for the factor ‘timepoint’, indicating that depression severity was reduced during treatment ($F_{1,46}=43.021$, $p<0.001$, $\eta^2_p=0.483$). Mean and SE of the mean are displayed. B, Baseline; BDI, Beck Depression Inventory; W4, after week 4/20 sessions of treatment.

response rates were equally distributed (BDI: 25.0 vs 25.0 (%), $\chi^2_1=0.000$, $p=1.000$, $\varphi=0.000$).

DISCUSSION

A previous randomised trial demonstrated similar effectiveness of ‘Beam F3’ and ‘5.5 cm rule’ targeting in rTMS treatment of depression.⁶ Our retrospective analyses of real-world clinical data complement these findings by showing that the ‘Beam F3’ method is not superior to the ‘6 cm rule’ and that ‘adjusted Beam F3’ does not outmatch the original ‘Beam F3’ method in terms of clinical outcome. This study provides unique data showing similar depression symptom improvement among three common scalp-based heuristics for TMS coil positioning. Based on our results, the number of participants needed to achieve 80% power was determined to be between ≈ 1400 and $\approx 872\,000$ for the outcome of per cent change in depression scales (online supplemental file 1). Even if group differences could be detected with such enormous sample sizes, this would be unlikely to translate into clinically meaningful differences between targeting strategies. This relative robustness of clinical efficacy against various scalp-based targeting heuristics may be due to interindividual neuroanatomical variability in scalp-cortex correspondence. However, there is also no clear evidence that target localisation using individual, structural MRI-guided neuronavigation improves treatment outcome.⁷ In contrast, evidence is accumulating that individualised functional connectivity-guided precision may be crucial for the identification of the optimal rTMS treatment site for depression and boost treatment response.⁸ Our results indicate that enhancing targeting precision via scalp-based heuristics does not affect treatment outcome, and thus, there is no need for clinicians to switch from their familiar to an ‘advanced’ approach among these common targeting heuristics.

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Competing interests None.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by the local Ethics Committee at RWTH Aachen University (EK 23-343). Participants gave informed consent to participate in the study before taking part.

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