Data supplement to Diefenbach et al. Repetitive transcranial magnetic stimulation for generalised anxiety disorder: pilot randomised, double-blind, sham-controlled trial. Br J Psychiatry doi: 10.1192/bjp.bp.115.168203

Online supplement DS1

**Competers sample**

*Completers sample baseline characteristics*

There were no differences between the active and sham groups on baseline demographic or clinical characteristics (See Table DS1).

**Table DS1**. Demographic and Clinical Characteristics by Group for Completers sample

| Characteristic | Active ($n$ = 9) | Sham ($n$ = 10) | Test |
|---|---|---|---|
| Age | 46.44 (10.81) | 41.40 (14.07) | $t$ = 0.87 |
| N (%) Women | 8 (88.9%) | 7 (70.0%) | $\chi^2$ = 1.02 |
| N (%) White | 9 (100%) | 10 (100%) | Not computed |
| N (%) Non-Hispanic | 9 (100%) | 10 (100%) | Not computed |
| N (%) with High School diploma | 9 (100%) | 10 (100%) | Not computed |
| N (%) Working | 6 (66.7%) | 6 (60.0%) | $\chi^2$ = 0.09 |
| N (%) Married | 6 (66.7%) | 7 (70.0%) | $\chi^2$ = 0.02 |
| CGI-Severity | 5.11 (0.78) | 4.50 (0.71) | $t$ = 1.78 |
| HRSA | 24.89 (5.23) | 21.10 (3.98) | $t$ = 1.79 |
| PSWQ | 69.67 (5.41) | 62.10 (10.55) | $t$ = 1.93 |
| HRSD | 14.67 (3.40) | 13.40 (2.31) | $t$ = 0.96 |

| | | | |
|---|---|---|---|
| DASS-Depression | 15.33 (10.98) | 13.50 (8.38) | $t$ = 0.41 |
| N (%) Taking psychotropic meds | 6 (66.7%) | 7 (70.0%) | $\chi^2$ = 0.02 |
| N (%) Any comorbid disorder | 6 (66.7%) | 6 (60.0%) | $\chi^2$ = 0.09 |
| N (%) Comorbid anxiety disorder | 3 (33.3%) | 4 (40.0%) | $\chi^2$ = 0.09 |
| N (%) Comorbid depressive disorder | 5 (55.6%) | 3 (30.0%) | $\chi^2$ = 1.27 |

*Note*. all tests $p < .05$; $t$ $df = 17$; $\chi^2$ $df = 1$, N = 19; CGI-Severity = Clinical Global Impression-Severity Scale; HRSA = Hamilton Rating Scale for Anxiety; PSWQ = Penn State Worry Questionnaire; HRSD = Hamilton Rating Scale for Depression; DASS-Depression = Depression Anxiety Stress Scales Depression Subscale

*Completers sample data analyses*

*Data Analytic Plan.* Patient attrition ($n$ = 1) at the 3-month follow-up caused unequal sample sizes across time. Thus, in order to include all available data and maximize power, separate 2 condition (active versus sham) by 2 time repeated measures analysis of variance (ANOVAs) were conducted: 1) with pretreatment and posttreatment as time variables and 2) with pretreatment and follow-up as time variables. The primary statistic of interest was the condition by time interaction effect and statistically significant interactions were followed by within-group paired *t*–tests. Within-group effect sizes (Cohen's *d*) are also presented and interpreted as 0.30 = small, 0.50 = medium, and 0.08 = large.[41] Given that this is a pilot study with small samples, statistical trends ($p < .10$) are also reported for future hypothesis generation purposes.

*Posttreatment Results.* Table DS2 displays descriptive statistics and paired *t*-tests of outcome variables and effect sizes for treatment completers at posttreatment. For the HRSA there was a significant effect of time [$F$ (1, 17) = 56.89, $p < .001$] and group by time interaction [$F$ (1, 17) = 6.49, $p < .05$]. This interaction resulted from a larger improvement in active versus sham,

although it should be noted that HRSAS effect sizes for both treatment conditions were large and statistically significant. Regarding secondary symptoms, there was a significant improvement over time for the DASS-DEP [$F$ (1, 17) = 6.23, $p < .05$] and HRSD [$F$ (1, 17) = 15.92, $p < .001$], and a trend for the PSWQ [$F$ (1, 17) = 4.21, $p = .056$]. None of the group by time interaction effects were statistically significant for secondary symptoms, although there was a trend toward interaction effects for the HRSD [$F$ (1, 17) = 3.83, $p = .067$] and PSWQ [$F$ (1, 17) = 3.26, $p = .089$]. In addition, a review of effect sizes indicated larger improvements in secondary symptoms for active ($d$ range = moderate to large effects) versus sham ($d$ range = small to moderate effects).

*3-Month Follow-up Results.* Means, standard deviations, paired $t$-tests, and effect sizes of outcome variables for participants completing 3-month follow-up are displayed in Table DS2. A significant time effect suggested overall improvements in anxiety [HRSA $F$ (1, 16) = 26.22, $p < .001$], worry [PSWQ $F$ (1, 16) = 21.43, $p < .001$], and depressive symptoms [HRSD $F$ (1, 16) = 8.14, $p < .05$; DASS-DEP $F$ (1, 16) = 5.19, $p < .05$]. Significant treatment condition by time interactions were also found for anxiety [HRSA $F$ (1, 16) = 16.37, $p = .001$], worry [PSWQ $F$ (1, 16) = 5.64, $p < .05$] and clinician-rated [HRSD $F$ (1, 16) = 10.55, $p < .01$], but not self-reported depressive symptoms [DASS-DEP $F$ (1, 16) = 1.50, $p > .05$]. The interactions occurred due to large (all $d$s $\geq 0.80$) and statistically significant improvements in the active group with nonsignificant, and smaller, more variable effect sizes ($d$ range = negligible to moderate) in sham.

*Additional references*

41 Cohen J (1988): *Statistical power analysis for the behavioral sciences*. 2nd ed. Hillsdale, NJ: Lawrence Erlbaum Associates.

Table DS2. Completers Sample Means, Standard Deviations, Paired *t*-tests and Effect Sizes for Outcome Variables

| Variable | Treatment Condition | Posttreatment Completers | | | | 3MFU Completers | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Pre | Post | *t* | *d* pre-post [95% CI] | Pre | 3MFU | *t* | *d* pre-FU [95% CI] |
| HRSA | Sham | 21.10 (3.98) | 14.50 (5.13) | 4.68*** | 1.48 [0.55 – 2.38] | 21.44 (4.07) | 19.56 (7.58) | 1.26 | 0.40 [-0.26 – 1.03] |
| | Active | 24.89 (5.23) | 11.56 (6.50) | 5.78*** | 1.93 [0.78 – 3.04] | 24.89 (5.23) | 8.78 (8.33) | 5.06*** | 1.79 [0.62 – 2.92] |
| PSWQ | Sham | 62.10 (10.55) | 61.60 (9.11) | 0.30 | 0.09 [-0.53 – 0.71] | 63.33 (10.39) | 58.11 (9.97) | 2.12 | 0.71 [-0.05 – 1.43] |
| | Active | 69.67 (5.40) | 61.89 (10.30) | 2.02 | 0.67 [-0.07 –1.39] | 69.67 (5.40) | 53.44 (9.89) | 4.13** | 1.46 [0.42 – 2.46] |
| HRSD | Sham | 13.40 (2.32) | 11.50 (3.71) | 2.48* | 0.78 [0.05 – 1.48] | 13.78 (2.11) | 14.33 (6.16) | -0.30 | -0.10 [-0.56 – 0.75] |
| | Active | 14.67 (3.39) | 9.11 (5.15) | 3.12* | 1.04 [0.20 – 1.84] | 14.67 (3.39) | 6.11 (5.32) | 4.02** | 1.42 [0.39 – 2.41] |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| DASS-DEP | Sham | 13.50 (8.38) | 10.60 (7.27) | 2.37* | 0.75 [0.03 – 1.44] | 13.67 (8.87) | 10.89 (12.58) | 0.86 | 0.29 [-0.39 – 0.95] |
| | Active | 15.33 (10.98) | 8.67 (10.14) | 1.74 | 0.58 [-0.15 – 1.28] | 15.33 (10.97) | 6.11 (11.09) | 2.21 | 0.78 [-0.04 – 1.56] |

*Note*. Active $n = 9$ for pretreatment, posttreatment, and 3 month follow-up. Sham $n = 10$ for pre-to-posttreatment analyses and $n = 9$ for pre-to-3-month follow-up analyses. * $p < .05$, ** $p < .01$, *** $p < .001$. FU = follow-up; HRSA = Hamilton Rating Scale for Anxiety; PSWQ = Penn State Worry Questionnaire; HRSD = Hamilton Rating Scale for Depression; DASS-DEP = Depression Anxiety Stress Scales-Depression Subscale; CI = confidence interval.

Figure DS1. Consort Diagram

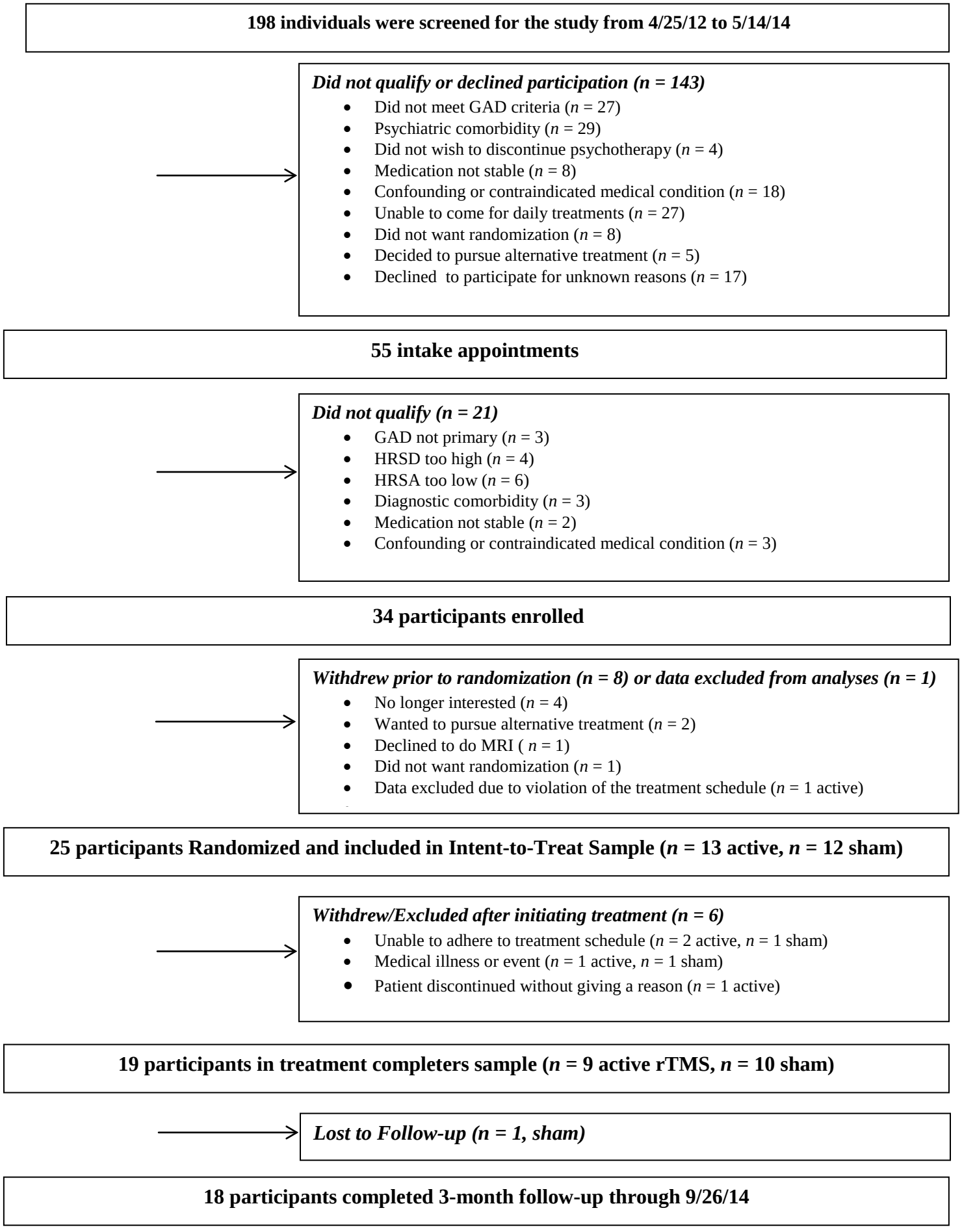

**Figure DS2. CONSORT Checklist**

| Section/Topic | Item No | Checklist item | Reported on page No |
|---|---|---|---|
| **Title and abstract** | | | |
| | 1a | Identification as a randomised trial in the title | 1 |
| | 1b | Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts) | 1 |
| **Introduction** | | | |
| Background and objectives | 2a | Scientific background and explanation of rationale | 1-2 |
| | 2b | Specific objectives or hypotheses | 2 |
| **Methods** | | | |
| Trial design | 3a | Description of trial design (such as parallel, factorial) including allocation ratio | 3 |
| | 3b | Important changes to methods after trial commencement (such as eligibility criteria), with reasons | 3 |
| Participants | 4a | Eligibility criteria for participants | 2 |
| | 4b | Settings and locations where the data were collected | 3 |
| Interventions | 5 | The interventions for each group with sufficient details to allow replication, including how and when they were actually administered | 2-3 |
| Outcomes | 6a | Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed | 2-3 |
| | 6b | Any changes to trial outcomes after the trial commenced, with reasons | N/A |
| Sample size | 7a | How sample size was determined | 3 |
| | 7b | When applicable, explanation of any interim analyses and stopping guidelines | N/A |
| Randomisation: | | | |
| Sequence generation | 8a | Method used to generate the random allocation sequence | 3 |
| | 8b | Type of randomisation; details of any restriction (such as blocking and block size) | 3 |
| Allocation concealment mechanism | 9 | Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned | 3 |
| Implementation | 10 | Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions | 3 |
| Blinding | 11a | If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how | 3 |

| | | | |
|---|---|---|---|
| | 11b | If relevant, description of the similarity of interventions | 2 |
| Statistical methods | 12a | Statistical methods used to compare groups for primary and secondary outcomes | 3 |
| | 12b | Methods for additional analyses, such as subgroup analyses and adjusted analyses | 3 |
| **Results** | | | |
| Participant flow (a diagram is strongly recommended) | 13a | For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome | Figure DS1 |
| | 13b | For each group, losses and exclusions after randomisation, together with reasons | Figure DS1 |
| Recruitment | 14a | Dates defining the periods of recruitment and follow-up | Figure DS1 |
| | 14b | Why the trial ended or was stopped | N/A |
| Baseline data | 15 | A table showing baseline demographic and clinical characteristics for each group | Table 1, Table DS1 |
| Numbers analysed | 16 | For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups | 3 |
| Outcomes and estimation | 17a | For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval) | Table 2, Table DS2 |
| | 17b | For binary outcomes, presentation of both absolute and relative effect sizes is recommended | NR |
| Ancillary analyses | 18 | Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory | 4-5 |
| Harms | 19 | All important harms or unintended effects in each group (for specific guidance see CONSORT for harms) | 4, Table 3 |
| **Discussion** | | | |
| Limitations | 20 | Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses | 6 |
| Generalisability | 21 | Generalisability (external validity, applicability) of the trial findings | 5-6 |
| Interpretation | 22 | Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence | 5-6 |
| **Other information** | | | |
| Registration | 23 | Registration number and name of trial registry | 3 |
| Protocol | 24 | Where the full trial protocol can be accessed, if available | N/A |
| Funding | 25 | Sources of funding and other support (such as supply of drugs), role of funders | 6 |

Note: N/A = not applicable. NR = not reported

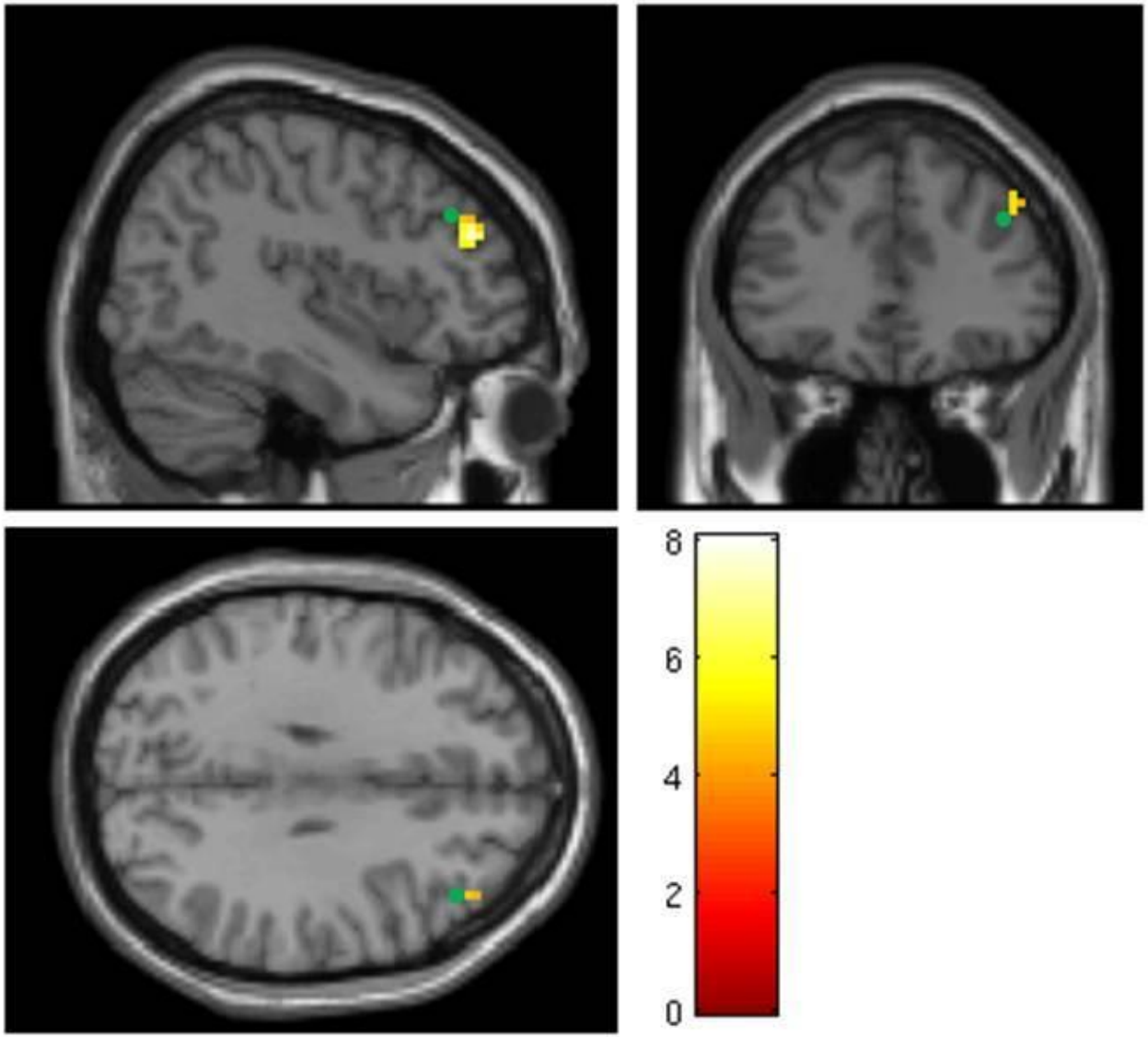


**Figure DS3 A Group (rTMS vs. Sham) × Time (pre- vs. posttreatment) interaction in right DLPFC during the gambling decision making fMRI task ($p < 0.05$ uncorrected, $k = 30$). The green dot represents the point of rTMS stimulation.**