Supplementary Online Content


**eAppendix.** Methods and Results

**eReferences.**

**eTable 1.** Physiotherapy Evidence Database (PEDro) Scale

**eTable 2.** rTMS Effects for Different Sham-rTMS Approaches

**eTable 3.** Risk of Bias Assessment in Individual Studies

**eFigure 1.** Flow Diagram

**eFigure 2.** Funnel Plot of Standard Error by Effect Size (SMD)

This supplementary material has been provided by the authors to give readers additional information about their work.
eAppendix. Methods and Results

Search Strategies

<table>
<thead>
<tr>
<th>Database</th>
<th>Search strategy</th>
<th>Items found</th>
</tr>
</thead>
<tbody>
<tr>
<td>PubMed</td>
<td>(parkinson's disease&gt;Title/Abstract) AND (((repetitive transcranial magnetic stimulation&gt;Title/Abstract) OR rTMS&gt;Title/Abstract)) OR repetitive TMS&gt;Title/Abstract)</td>
<td>155</td>
</tr>
<tr>
<td>Web of Science</td>
<td>(TOPIC: (Parkinson's disease) OR TITLE: (Parkinson's disease)) AND TITLE: (repetitive transcranial magnetic stimulation) OR TOPIC: (repetitive transcranial magnetic stimulation) OR TITLE: (repetitive TMS) OR TOPIC: (repetitive TMS) OR TITLE: (rTMS) OR TOPIC: (rTMS)</td>
<td>667</td>
</tr>
<tr>
<td>EMBASE</td>
<td>'parkinsons disease' and ('repetitive transcranial magnetic stimulation' or 'rTMS' or 'repetitive TMS')</td>
<td>315</td>
</tr>
<tr>
<td>SCOPUS</td>
<td>(TITLE-ABS-KEY(parkinson's disease)) AND ((TITLE-ABS-KEY(repetitive transcranial magnetic stimulation)) OR (TITLE-ABS-KEY(repetitive tms)) OR (TITLE-ABS-KEY(rtms)))</td>
<td>201</td>
</tr>
<tr>
<td>Cochrane Library</td>
<td>parkinson's disease and repetitive transcranial magnetic stimulation</td>
<td>865</td>
</tr>
</tbody>
</table>
Search Results

Step 1: Records identified through database searching \((n = 155 + 667 + 315 + 201 + 865 = 2203)\)

Step 2: Additional records identified through other sources \((n = 1)\)

Step 3: Full-text articles assess for eligibility \((n = 60)\)

Step 4: Among the 60 potentially eligible studies, 40 full-text articles were excluded because of the following reasons:

- UPDRS-III not included in the article as an outcome measure for the rTMS effect \((n = 16)\)
  - \(^3,6,9,11,14,16,17,19,23-26,42,51,52,57\)
- Not randomized sham-controlled trials \((n = 14)\)
  - \(^1,4,28-31,35-38,48,50,56,58\)
- Did not directly examine rTMS effect \((n = 4)\)
  - Testing difference between “active-rTMS + placebo drug” and “drug + sham-rTMS”\(^44,46\)
  - Varied rTMS intensity and duration of train to test safety\(^15\)
  - Theta burst stimulation included in the rTMS treatment protocol\(^33\)
- Statistical data not available for meta-analysis\(^2,49\)
- Single-case study\(^10,20\)
- Not idiopathic PD\(^13\)
- Article not written in English\(^60\)

Step 5: Studied included in meta-analysis \((n = 20)\)
  - \(^5,7,8,12,18,21,22,27,32,34,39-41,43,45,47,53-55,59\)
Results. Analysis of Quality of Individual Studies

The results showed that eight studies were of excellent methodological quality (PEDro scale 11/11). Ten studies were of good methodological quality (8/11 – 10/11). One study was of fair methodological quality (7/11). The results were summarized in eTable 3. In order to assess whether the rigor of studies would influence the overall rTMS effect size, we conducted the following three different analyses:

First, we removed one study with a PEDro score of 7 (i.e., keeping excellent and good-quality studies), and found that the effect size (or SMD) increased from 0.46 (N = 19) to 0.48 (N = 18, standard error = 0.09, 95% CI = [0.29, 0.64]). Second, we removed 11 studies with a PEDro score less than 11 (i.e., only keeping excellent-quality studies with a PEDro score of 11). The data showed that the SMD increased from 0.46 (N = 19) to 0.49 (N = 8, standard error = 0.15, 95% CI = [0.21, 0.78]). Third, we ran a meta-regression with the PEDro score as a predictor. The results showed that no significant correlation between the PEDro score and the SMD was found, $r = 0.06, p = 0.52$. The findings suggest that although better-quality studies had a tendency to increase the rTMS effect, the correlation between quality score and effect size was not significant.
eReferences


27. Sedlackova S, Rektorova I, Srovnalova H, Rektor I. Effect of high frequency repetitive transcranial magnetic stimulation on reaction time, clinical features and cognitive...


49. Okabe S, Ugawa Y, Kanazawa I. 0.2-Hz repetitive transcranial magnetic stimulation has no add-on effects as compared to a realistic sham stimulation in Parkinson's disease. *Mov Disord.* Apr 2003;18(4):382-388.


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Table 1. Physiotherapy Evidence Database (PEDro) Scale

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Eligibility criteria were specified.</td>
</tr>
<tr>
<td>2</td>
<td>Participants were randomly allocated to groups.</td>
</tr>
<tr>
<td>3</td>
<td>Allocation was concealed.</td>
</tr>
<tr>
<td>4</td>
<td>The groups were similar at baseline regarding the most important prognostic indicators.</td>
</tr>
<tr>
<td>5</td>
<td>There was blinding of all participants.</td>
</tr>
<tr>
<td>6</td>
<td>There was blinding of all personnel who administered the intervention.</td>
</tr>
<tr>
<td>7</td>
<td>There was blinding of all assessors who measures at least 1 key outcome.</td>
</tr>
<tr>
<td>8</td>
<td>Measures of at least 1 key outcome were obtained from more than 85% of the participants initially allocated to groups.</td>
</tr>
<tr>
<td>9</td>
<td>All participants for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least 1 key outcome were analyzed by “intention to treat.”</td>
</tr>
<tr>
<td>10</td>
<td>The results of between-group statistical comparisons are reported for at least 1 key outcome.</td>
</tr>
<tr>
<td>11</td>
<td>The study provides both point measures and measures of variability for at least 1 key outcome.</td>
</tr>
</tbody>
</table>
eTable 2. rTMS effects for different sham-rTMS approaches

<table>
<thead>
<tr>
<th>Type</th>
<th>No. of studies</th>
<th>SMD</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Back-surface coil</td>
<td>1</td>
<td>1.18</td>
<td>[0.07, 2.28]</td>
<td>0.04</td>
</tr>
<tr>
<td>Active-rTMS at occipital regions</td>
<td>3</td>
<td>0.62</td>
<td>[0.08, 1.16]</td>
<td>0.03</td>
</tr>
<tr>
<td>Tilted coil</td>
<td>6</td>
<td>0.60</td>
<td>[0.25, 0.96]</td>
<td>0.001</td>
</tr>
<tr>
<td>Sham coil</td>
<td>3</td>
<td>0.44</td>
<td>[-0.11, 1.00]</td>
<td>0.12</td>
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<tr>
<td>Inactive coil with stimulation sound</td>
<td>1</td>
<td>0.43</td>
<td>[-0.51, 1.36]</td>
<td>0.37</td>
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<tr>
<td>Realistic coil</td>
<td>3</td>
<td>0.34</td>
<td>[0.06, 0.61]</td>
<td>0.02</td>
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<tr>
<td>Active coil on top of an inactive coil</td>
<td>2</td>
<td>0.30</td>
<td>[-0.30, 0.90]</td>
<td>0.33</td>
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### eTable 3. Risk of bias assessment in individual studies

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<tr>
<th>Study</th>
<th>Selection</th>
<th>Performance</th>
<th>Detection</th>
<th>Attrition&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Reporting</th>
<th>Carry-over&lt;sup&gt;b&lt;/sup&gt;</th>
<th>PEDro</th>
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<tr>
<td>Siebner et al.&lt;sup&gt;55&lt;/sup&gt;, 2000</td>
<td>+</td>
<td>+</td>
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<td>Boylan et al.&lt;sup&gt;54&lt;/sup&gt;, 2001</td>
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<td>?&lt;sup&gt;c&lt;/sup&gt;</td>
<td>+</td>
<td>+</td>
<td>?&lt;sup&gt;d&lt;/sup&gt;</td>
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<td>+</td>
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<td>N/A</td>
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<td>+</td>
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<tr>
<td>Maruo et al.,&lt;sup&gt;57&lt;/sup&gt; 2013</td>
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<td>11/11</td>
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<td>Shirota et al.,&lt;sup&gt;8&lt;/sup&gt; 2013</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>N/A</td>
<td>11/11</td>
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</tr>
<tr>
<td>Nardone et al.,&lt;sup&gt;5&lt;/sup&gt; 2014</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>N/A</td>
<td>+</td>
<td>?&lt;sup&gt;f&lt;/sup&gt;</td>
<td>8/11</td>
</tr>
</tbody>
</table>

Note. The Cochrane tool classifies studies as having low (+), high (-), or unclear (?) risk of bias in the following domains: selection bias, performance bias, detection bias, attrition bias, reporting bias, and carry-over effect. The PEDro scale was used to evaluate the number of items that met the criteria for quality assessment of RCTs. We considered a PEDro score of ≥ 8 to represent a high-quality study, a score of 6 and 7 a moderate-quality study, and a score of ≤ 5 a low-quality study.<sup>61</sup>  

<sup>a</sup>Assessment of attrition bias is only relevant for parallel RCTs;  
<sup>b</sup>Assessment of carry-over bias is only relevant for cross-over RCTs;  
<sup>c</sup>Not clear whether participants were randomized into different groups;  
<sup>d</sup>Not clear whether there was no systematic
difference between groups in withdrawals; *Not clear whether patients were blinded; †Not clear whether there was a carry-over effect; ‡Not clear whether patients, personnel, and outcome assessors were blinded.
eFigure 1. Flow Diagram. The search and selection procedure that was used for this meta-analysis. Diagram adapted from Moher et al.\textsuperscript{62} rTMS indicates repetitive transcranial magnetic stimulation; UPDRS-III, Unified Parkinson's Disease Rating Scale III.

Records identified through database searching
(n = 2203)

Additional records identified through other resources
(n = 1)

Full-text articles assess for eligibility
(n = 60)

Studies included in meta-analysis
(n = 20)

Full-text articles excluded (n = 40):
- UPDRS-III not included as an outcome measure (n = 16)
- Not randomized sham-controlled trials (n = 14)
- Data not available for meta-analysis (n = 2)
- Not idiopathic PD (n = 1)
- Single-case study (n = 2)
- Did not directly examine rTMS effect (n = 4)
- Article not written in English (n = 1)
eFigure 2. Funnel plot of standard error by effect size (SMD). The funnel plot was plotted with SMD on the X axis and the standard error on the Y axis.