Noninvasive Brain Stimulation

Does it work?
Motor evoked potential ( MEP)
Simplified schema for TMS action in the motor cortex

Cortex

Horizontal axons (excitatory)

Inhibitory interneurons

Sites of TMS action

Peripheral nerve and muscle
Increased excitability after high-frequency rTMS
Effect of 1 Hz rTMS on M1 excitability
File drawer papers: 144/153
Formal power calculations 20%
Added subjects after setting sample size 15%

Found effects as reported
Continuous theta burst TMS 45%
Intermittent theta burst TMS 45%
Low frequency TMS 60%
High frequency TMS 59%

No effect of years of experience
RESEARCH ARTICLE

The Use and Abuse of Transcranial Magnetic Stimulation to Modulate Corticospinal Excitability in Humans

Martin E. Héroux¹,², Janet L. Taylor¹,², Simon C. Gandevia¹,²,*

¹ Neuroscience Research Australia, Randwick, NSW, Australia; ² University of New South Wales, Randwick, NSW, Australia

Table 1. Prevalence of questionable research practices.

<table>
<thead>
<tr>
<th>Questionable research practices</th>
<th>Others [count(%)]</th>
<th>Self [count(%)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screen for ‘responders’ to a TMS protocol</td>
<td>38 (68)</td>
<td>18 (38)</td>
</tr>
<tr>
<td>Drop data points based on a gut feeling</td>
<td>18 (38)</td>
<td>6 (13)</td>
</tr>
<tr>
<td>Exclude data after looking at impact on results</td>
<td>14 (30)</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Not report all experimental conditions</td>
<td>19 (40)</td>
<td>10 (21)</td>
</tr>
<tr>
<td>Selectively report outcomes</td>
<td>23 (49)</td>
<td>5 (11)</td>
</tr>
<tr>
<td>Selectively report time points</td>
<td>14 (30)</td>
<td>5 (11)</td>
</tr>
<tr>
<td>Selectively report sub-groups of subjects</td>
<td>18 (38)</td>
<td>8 (17)</td>
</tr>
<tr>
<td>Reject ‘outliers’ without statistical support</td>
<td>19 (30)</td>
<td>10 (21)</td>
</tr>
</tbody>
</table>
Transient effects – summary

$J = 2\text{mA}$

$E < 0.5 \text{ V/m}$

$0.1\text{mV}$

→ 1% firing rate
→ 1% synaptic efficacy
→ 1ms timing → entrainment

Reato, *Frontiers in Human Neuroscience*, 2013
Detailed models of current flow

- Maximum not always under the electrode
- Polarity inevitably mixed

(c) Lucas C. Parra, 9/29/16

Datta, Brain Stimulation, 2009
Rahman, J Physiology, 2013
Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation

M. A. Nitsche and W. Paulus

Department of Clinical Neurophysiology, University of Goettingen, Robert Koch Strasse 40, 37075 Goettingen, Germany
**Motor Systems**

Direct currents (DC) applied directly to central nervous system structures produce substantial and long-lasting effects in animal experiments. We tested the functional effects of very weak scalp DC (<0.5 mA, 7 s) on the human motor cortex by assessing the changes in motor potentials evoked by transcranial magnetic brain stimulation. We performed four different experiments in 15 healthy volunteers. Our findings led to the conclusion that such weak (<0.5 mA) anodal scalp DC, alternated with a cathodal DC, significantly depresses the excitability of the human motor cortex, providing evidence that a small electric field crosses the skull and influences the brain. A possible mechanism of action of scalp DC is the hyperpolarization of the superficial excitatory interneurones in the human motor cortex. *NeuroReport* 9: 2257–2260 © 1998 Rapid Science Ltd.

**Key words**: Cortical interneurones; Corticomotoneuronal connection; Descending volley; Direct current; Motor cortex; Motor potentials; Polarization; Transcranial magnetic brain stimulation

**NeuroReport** 9, 2257–2260 (1998)

**Polarization of the human motor cortex through the scalp**

Alberto Priori,¹ Alfredo Berardelli,¹,²,CA Sabine Rona,¹,² Neri Accornero¹,² and Mario Manfredi¹,²

¹Dipartimento di Scienze Neurologiche, Università degli Studi di Roma ‘La Sapienza’, Viale dell’Università 30, 00185 Roma, Italy
²Istituto Neuromed, Pozzilli (IS), Italy
Intra-Subject Consistency and Reliability of Response Following 2 mA Transcranial Direct Current Stimulation

Katherine Dyke a, Soyoung Kim a, Georgina M. Jackson b, Stephen R. Jackson a,*
Intra-Subject Consistency and Reliability of Response Following 2 mA Transcranial Direct Current Stimulation

Katherine Dyke a, Soyoung Kim a, Georgina M. Jackson b, Stephen R. Jackson a,*
Response variability of different anodal transcranial direct current stimulation intensities across multiple sessions

Claudia Ammann, Martin A. Lindquist, Pablo A. Celnik

A

B

**fficent session mean**
Response variability of different anodal transcranial direct current stimulation intensities across multiple sessions

Claudia Ammann\textsuperscript{a}, Martin A. Lindquist\textsuperscript{b}, Pablo A. Celnik\textsuperscript{a, *}
Questionable science and reproducibility in electrical brain stimulation research

Martin E. Héroux1,2, Colleen K. Loo3,4,5, Janet L. Taylor1,2, Simon C. Gandevia1,2,6*

1 Neuroscience Research Australia, Randwick, NSW, Australia, 2 School of Medical Sciences, University of New South Wales, Sydney, NSW, Australia, 3 School of Psychiatry, University of New South Wales, Sydney, NSW, Australia, 4 Black Dog Institute, University of New South Wales Sydney, NSW, Australia, 5 Department of Psychiatry, St. George Hospital, Sydney, NSW, Australia, 6 Prince of Wales Clinical School, University of New South Wales, Sydney, NSW, Australia

Table 2. Sample size determination.

<table>
<thead>
<tr>
<th></th>
<th>Total studies (n [%]) *</th>
<th>Respondents (%) †</th>
<th>Audit papers (%) ‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Power calculation</td>
<td>426 [26]</td>
<td>61</td>
<td>6</td>
</tr>
<tr>
<td>Pilot data</td>
<td>126 [8]</td>
<td>32</td>
<td>1</td>
</tr>
<tr>
<td>Sample size from published paper</td>
<td>403 [25]</td>
<td>69</td>
<td>0</td>
</tr>
<tr>
<td>Personal experience</td>
<td>364 [22]</td>
<td>38</td>
<td>0</td>
</tr>
<tr>
<td>How data are looking</td>
<td>74 [5]</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>Stop study early—no effect</td>
<td>55 [3]</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>Stop study early—effect</td>
<td>21 [1]</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Allow more samples to be collected</td>
<td>130 [8]</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td>No strategy</td>
<td>41 [3]</td>
<td>11</td>
<td>93</td>
</tr>
</tbody>
</table>
Questionable science and reproducibility in electrical brain stimulation research

Martin E. Héroux\textsuperscript{1,2}, Colleen K. Loo\textsuperscript{3,4,5}, Janet L. Taylor\textsuperscript{1,2}, Simon C. Gandevia\textsuperscript{1,2,6*}

\textsuperscript{1} Neuroscience Research Australia, Randwick, NSW, Australia, \textsuperscript{2} School of Medical Sciences, University of New South Wales, Sydney, NSW, Australia, \textsuperscript{3} School of Psychiatry, University of New South Wales, Sydney, NSW, Australia, \textsuperscript{4} Black Dog Institute, University of New South Wales Sydney, NSW, Australia, \textsuperscript{5} Department of Psychiatry, St. George Hospital, Sydney, NSW, Australia, \textsuperscript{6} Prince of Wales Clinical School, University of New South Wales, Sydney, NSW, Australia

Table 3. Prevalence of questionable research practices.

<table>
<thead>
<tr>
<th>Questionable research practices</th>
<th>Others (%)</th>
<th>Self (%)</th>
<th>Audit (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjust statistical analyses in order to optimise the results</td>
<td>43</td>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td>Not report all experimental conditions</td>
<td>36</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Screen whether subjects are responders and not report it</td>
<td>21</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Exclude data based on a gut feeling</td>
<td>21</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Exclude data after looking at impact on results</td>
<td>20</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Exclude trials or subjects without support of statistical analysis</td>
<td>22</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Selectively report outcomes</td>
<td>41</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>Selectively report time points</td>
<td>18</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Selectively report types of EBS used in study</td>
<td>12</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Selectively report sub-groups of subjects</td>
<td>24</td>
<td>14</td>
<td>0</td>
</tr>
</tbody>
</table>
Quantitative Review Finds No Evidence of Cognitive Effects in Healthy Populations From Single-session Transcranial Direct Current Stimulation (tDCS)

Jared Cooney Horvath *, Jason D. Forte, Olivia Carter

University of Melbourne, Melbourne School of Psychological Sciences, Redmond Barry Building, Melbourne, VIC 3010, Australia

Evidence that transcranial direct current stimulation (tDCS) generates little-to-no reliable neurophysiologic effect beyond MEP amplitude modulation in healthy human subjects: A systematic review

Jared Cooney Horvath *, Jason D. Forte, Olivia Carter

University of Melbourne, School of Psychological Sciences, Melbourne, VIC, Australia
Rigor and reproducibility in research with transcranial electrical stimulation: An NIMH-sponsored workshop

The problem

Put thing on head → Putative mechanism → Find effect
The problem

Put thing on head → Putative mechanism → Find effect

“Confirm” mechanism
The problem

```
Put thing on head

Putative mechanism

“Confirm” mechanism

Find effect

Propagate BS in literature
```
Shifts in connectivity during procedural learning after motor cortex stimulation: A combined transcranial magnetic stimulation/functional magnetic resonance imaging study

Adam Steel a, Sunbin Song b, Devin Bageac a, Kristine M. Knutson a, Aysha Keisler a, Ziad S. Saad c, Stephen J. Gotts d, Eric M. Wassermann a,* and Leonora Wilkinson a

Fig. 1 – Experimental design. Each participant underwent two TBS-fMRI sessions, during which they received either real or sham cTBS over M1. The order of stimulation conditions was counterbalanced. Experimental sessions occurred at least one week apart.
Targeted enhancement of cortical-hippocampal brain networks and associative memory

Jane X. Wang, Lynn M. Rogers, Evan Z. Gross, Anthony J. Ryals, Mehmet E. Dokucu, Kelly L. Brandstatt, Molly S. Hermiller, Joel L. Voss
Targeted enhancement of cortical-hippocampal brain networks and associative memory

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Reproduction

* - p < 0.05
Baseline Hippocampal FC predicts change in FC

Wang

Freedberg

Δ fMRI connectivity
Depends