Effects of Transcranial Direct Current Stimulation (TDCS) on Sleep-Dependent Memory Consolidation in Elderly Healthy Subjects

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No Effects of Slow Oscillatory Transcranial Direct Current Stimulation (tDCS) on Sleep-Dependent Memory Consolidation in Healthy Elderly Subjects

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Boosting slow oscillations during sleep potentiates memory

Lisa Marshall¹, Halla Helgadóttir¹, Matthias Mölle¹ & Jan Born¹

A bifrontal anodal slow oscillating tDCS with a frequency of 0.75 Hz during early slow wave sleep
• had a positive effect on overnight declarative memory consolidation
• increased EEG power in the slow oscillation and in the slow sleep spindle frequency band compared to sham so-tDCS
Basics of Sleep (Sleep Stages)

Two different types of sleep

Increase in slow wave activity
NonREM-sleep
- NREM1 / N1
- NREM2 / N2
- SWS / N3

Phases of activation
REM-Sleep / stage R
REM = Rapid Eye Movements

Dream sleep

Additionally stage Wake can be identified
Basics of Sleep (Sleep Stages: EEG Characteristics)

- W: Wake with Alpha
- N2: Stage 2
- S3: Stage 3
- S4: Stage 4
- R: REM

From Feinberg and Campbell (2010)

- Sleep spindles
- δ-waves with high amplitude low frequency
Declarative memories are temporarily encoded during the day and become reactivated during the night. Slow oscillations (<1 Hz) exert a temporal synchronizing influence on both hippocampal reactivations and thalamic spindle activity in order to ensure that both activities reach the neocortex nearly at the same time.
constant (c)-tDCS vs. slow oscillatory (so)-tDCS

From Bergmann et al. (2009)

- **c-tDCS:**
  Application of a constant current for a certain time

- **so-tDCS:**
  Application of an oscillating current for a certain time
  - if the stimulation signal resembles the ongoing brain activity (resonance), it enables an interaction with these endogeneous oscillatory brain activities
Participants

23 individuals (14 ♀; 9 ♂) participated (mean age: 69.3 years, SD= 8.0; age range: 60-90 years)

Inclusion criteria:
- age ≥ 60 years
- no sleep disturbances currently or in the past
- No irregular sleep-wake rhythm

Exclusion criteria:
- cognitive impairments
- CNS-active medications
- untreated medical condition
- any medical, neurological or psychiatric condition, which has a clinically significant effect on sleep and/or vigilance
- smoker
Study Design

1) Adaptation night to screen for sleep disturbances by polysomnography (Apnea-hypopnea Index >15; Periodic limb movement arousal Index > 15)

   ↓ 1 day

2) First experimental night (verum or sham stimulation)

   ↓ 1 week

3) Second experimental night (verum or sham stimulation)

Assignment of stimulation conditions followed a double-blind, randomised, cross-over design

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>18:30/19:15 – 21:00</td>
<td>Fixation of EEG and stimulation electrodes</td>
</tr>
<tr>
<td>21:00 – 22:30 (learning)</td>
<td>ct, mt</td>
</tr>
<tr>
<td>23:00 – 06:30 (sleep)</td>
<td>verum or sham stimulation (ct, mt)</td>
</tr>
<tr>
<td>07:00 – 08:00 (retrieval)</td>
<td>mt, ct</td>
</tr>
<tr>
<td>08:00 – 09:00</td>
<td>Removal of all electrodes</td>
</tr>
</tbody>
</table>

c_t = control tasks; m_t = memory tasks
Memory Tasks

• **word pair test (declarative)**
  - 54 German word pairs (e.g. instrument – trumpet)
  - 2 different word lists
  - learning criterion: 60 % correct responses

• **finger-tapping (procedural)**
  - five-digit sequences
  - 2 different sequences
  - 12 x 30 sec sessions

1 1 2 3 4
* - * - * - _ - _
- 12 x 30 sec sessions
DC Stimulator / Electrode Positions

„eldith“ DC stimulator plus (neuroConn GmbH,Ilmenau, Germany)

red = EEG electrodes; brown = reference; blue = ground; green = stimulation electrodes
Stimulation Paradigm


- Type of stimulation: sinus
- Current strength: 0.26 mA
- Current density: 0.331 mA/cm²
- Frequency: 0.75 Hz
- Fade in/out [s]: 2 * 8 s

1 cycle = 1.33 s = 0.75 Hz

6 cycles = 8 s

215 cycles
Data Analysis

- performances in memory tasks

- sleep scoring of the five stimulation free intervals

- sleep spindle density (slow and fast sleep spindles) within the five stimulation free intervals

- EEG power in the following frequency bands (calculated as differences between the stimulation free intervals and a 1 minute baseline interval before stimulation):
  - 0.5-1 Hz
  - 1-1.5 Hz
  - 1-4 Hz
  - 8-12 Hz
  - 12-15 Hz
Results - Declarative Memory Task

A

- Word pairs
- Evening vs. Morning
- P < 0.001

- Overnight change in word pairs
- Verum vs. Sham
- P = 0.076

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Results - Procedural Memory Task

B

$P = 0.001$

$P = 0.011$

n.s.

Correct sequences

Overnight change in correct sequences

evening morning

Verum

Sham

Verum

Sham

Evening morning
### Results – Sleep Scoring / Spindle Analysis

<table>
<thead>
<tr>
<th></th>
<th>Verum stimulation [mean ± SEM]</th>
<th>Sham stimulation [mean ± SEM]</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unidentified</td>
<td>0.9 ± 0.6</td>
<td>0.0 ± 0.0</td>
<td>ns&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Wake</td>
<td>61.3 ± 14.6</td>
<td>24.3 ± 7.7</td>
<td>0.018&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>REM</td>
<td>11.3 ± 6.5</td>
<td>7.8 ± 4.3</td>
<td>ns&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>NREM stage 1</td>
<td>30.9 ± 7.2</td>
<td>20.4 ± 6.5</td>
<td>ns&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>NREM stage 2</td>
<td>132.6 ± 16.2</td>
<td>152.6 ± 17.4</td>
<td>ns&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>NREM stage 3</td>
<td>38.7 ± 7.0</td>
<td>64.3 ± 12.8</td>
<td>0.030&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>NREM stage 4</td>
<td>23.5 ± 10.8</td>
<td>21.7 ± 7.9</td>
<td>ns&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>SWS</td>
<td>62.2 ± 14.4</td>
<td>86.1 ± 19.7</td>
<td>ns&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Total</td>
<td>299.1 ± 0.9</td>
<td>291.3 ± 4.3</td>
<td>ns&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> t-test for paired observations.

<sup>b</sup> Wilcoxon matched-pairs signed-ranks test.

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**Slow frontal and fast parietal spindle densities for both stimulation conditions.**

<table>
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<tr>
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<th>Sham stimulation [mean ± SEM]</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slow frontal spindle density</td>
<td>2.25 ± 0.30</td>
<td>2.24 ± 0.29</td>
<td>ns&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Fast parietal spindle density</td>
<td>2.99 ± 0.30</td>
<td>3.24 ± 0.36</td>
<td>ns&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Slow vs. fast: verum stimulation: \( P = 0.022^a \); sham stimulation: \( P = 0.002^a \).

SEM = standard error.

<sup>a</sup> t-test for paired observations.
Discussion

Deviating results could be explained:
- by fundamental changes in sleep architecture with age,
- As frequency and amplitude of the EEG decreases with age, it could be assumed that the stimulation signal might not have perfectly met ongoing brain oscillations in the elderly.
Outlook

• Focus of new tDCS study on

  ➢ Age-specific differences in sleep-dependent memory consolidation by adding a sample of young adults

  ➢ Gender-specific differences in sleep-dependent memory consolidation

• Collaboration with Theo Samaras

• Further suggestions on how to adjust the stimulation signal for the elderly?
Thank you for your attention!


