Transcranial electrical stimulation (tES): basics, mechanisms and its application in neurodegenerative diseases

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Physiological correlates of psychological and behavioural processes

- **stimuli**
  - visual
  - auditory
  - somatosensory
  - gustatory
  - olfactory
  - vegetative

- **perception**
- **behaviour**
- **motor activity**

- **cognition, motivation, emotion**

Modulation of cortical activity, and excitability in humans

Activity
- TMS
- rTMS
- PAS

Plasticity
- tDCS

Oscillations
- tACS
- tRNS
Primary action of DC-stimulation: modulation of resting membrane potential

Electrode positions:
- m = motor cortex;
- prm = premotor cortex;
- pom = post-motor cortex;
- oc = occipital;
- cS = contralateral forehead;
- cm = kontralateral motor cortex

MEP Amplitude with/without tDCS

- anodal stimulation
- cathodal stimulation

Rahman et al. 2013

AP threshold
tDCS in humans
Polarity-dependent excitability-modulation during tDCS

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- m = motor cortex
- prm = premotor cortex
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- oc = occipital
- cS = contralateral forehead
- cm = kontralateral motor cortex

Nitsche & Paulus 2000
After-effects of tDCS - plasticity
Conclusion 1

- Non-invasive brain stimulation allows to alter cortical activity, and excitability, including brain oscillations.

- Neuroplastic after-effects are accomplished by tDCS.

- These after-effects depend on the glutamatergic system.
Modulation of brain functions by electrical stimulation
Exploration of cognitive processes via tDCS – motor learning

Serial reaction time task (SRTT)

12 stimuli, 10 times repetition per block

Procedure
- Sequence
- Random order

Effect of sequence learning

Task routine
Motor learning – involved areas

**Initial Learning**

Honda et al. Brain 1998

**Consolidation**

Honda et al. Brain 1998

**tDCS over M1**


Premotor tDCS

Reaktionszeiten / Baseline
Working memory – performance alterations by tDCS

Fregni et al. Exp Brain Res 2005, Mannie et al. 2010
Working memory – network synchronisation improves performance

Polania et al. Curr Biology 2012
Conclusion II

- tES alters cognitive processes in healthy humans
- tDCS-induced neuroplasticity improves learning
- tDCS and tACS improve working memory performance
Application of tES in Alzheimer’s disease
Improvement of memory

- Double-blinded randomized, 15 patients
- Bilateral temporal, return electrode extracephalic
- 15 min tDCS, 1.5 mA
- Single session

Ferrucci et al. 2008
Improvement of memory

- Case report
- Anode T3, cathode Fp2
- 30 min tDCS twice daily
- tDCS over 6 consecutive days

<table>
<thead>
<tr>
<th>Test</th>
<th>Baseline Raw score/scaled score</th>
<th>Post-test 1 Raw score/scaled score</th>
<th>Post-test 2 Raw score/scaled score</th>
<th>Improvement (%) Baseline to Post-test 2</th>
<th>RCI Baseline to Post-test 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVLT Immediate Recall</td>
<td>21/15</td>
<td>31/37</td>
<td>27/35</td>
<td>28.57</td>
<td>1.44</td>
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<tr>
<td>CVLT-II Delayed Recall</td>
<td>4/-1.5</td>
<td>7/-1</td>
<td>7/-1</td>
<td>75.00</td>
<td>1.84</td>
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<tr>
<td>CVLT-II Recognition Total Hits</td>
<td>15/0.5</td>
<td>14/0</td>
<td>14/0</td>
<td>-6.67</td>
<td>-0.77</td>
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<td>CVLT-II Recognition False Positive</td>
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<td>15/4</td>
<td>15/4</td>
<td>0.00</td>
<td>0.04</td>
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<tr>
<td>D-KEFS Word Fluency</td>
<td>22/6</td>
<td>19/5</td>
<td>19/5</td>
<td>-13.64</td>
<td>-0.62</td>
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<td>Phonemic</td>
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<td>14/1</td>
<td>12/1</td>
<td>9.09</td>
<td>0.16</td>
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<td>D-KEFS Word-Fluency Categorical</td>
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<td>7/4</td>
<td>8/6</td>
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<td>WMS Attention Span</td>
<td>93</td>
<td>137</td>
<td>78</td>
<td>-16.13</td>
<td>-1.2</td>
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<td>TMT A</td>
<td>19</td>
<td>22</td>
<td>27</td>
<td>42.11</td>
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<td>MMSE</td>
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<td>73</td>
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<tr>
<td>GDS</td>
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<td>Richard-Campbell Sleep Questionnaire</td>
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<td>0</td>
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</table>

**Note:** Results from the California Verbal Learning Test II (CVLT-II) Immediate Recall are displayed as a T-score (normative mean = 50, SD = 10). CVLT-II Delayed Recall and CVLT-II Recognition are shown as Z-scores (normative mean = 0, SD = 1). The maximum score on the Clock-Drawing Test is five, and the highest score on the Mini Mental Status Exam (MMSE) is 30. The results of the Trail Making Test A (TMT A) are displayed in seconds. The cut-off score for GDS is >11. The Reliable Change Index (RCI) is a measure of statistical reliable change, in which ±1.645 is the commonly used cut-off score of clinical significance [7]. For the MMSE and Clock-Drawing, RCI was not estimated because of the lack of test-retest coefficients.
Improvement of memory

- Double-blinded randomized, 15 patients
- Anodes bilateral temporal, return electrode extracephalic
- 30 min tDCS once daily, 2 mA
- tDCS over 5 consecutive days
- Visual recognition task
General Cognitive functioning

- 34 patients
- All under memantine
- Parallel groups
- Anodal/cathodal/sham left DLPFC
- 25 min tDCS once daily
- tDCS over 10 consecutive workdays

Khedr et al. 2014
Conclusion III

- tDCS might have therapeutic potential in neurodegenerative diseases
- Results of some pilot studies are promising
- Knowledge about optimized protocols, and effect of tACS is missing
- RCTs are missing
- Currently not ready for clinical routine practice
Many thanks for your attention!