Combining tES and EEG

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With some slides provided by Mouhsin Shafi, MD., PhD.,
Beth Israel Deaconess Medical Center
Harvard Medical School
History – DC Stimulation in Cats

Creutzfeldt et al, 1962

- Motor and visual cortex neurons
- Surface positive (inward current) => Increased spiking
- Surface negative (outward current) => Decreases neuronal spiking

Effect of positive DC current on spontaneous neuron activity and EEG in the motor cortex

Figure adapted from Creutzfeldt et al., 1962.
History – tDCS in Humans

Figure adapted from Nitsche & Paulus, 2000

Nitsche & Paulus, 2000

- Motor Cortex
- Changes in cortical excitability
- TMS-EMG used to demonstrate changes in cortical excitability
**SIDE NOTE: TMS-EMG**

Transcranial Magnetic Stimulation + Electromyography

Figure Adapted from Farzan F – Neuromethods
tDCS Effects – Session

Figure Adapted from Nitsche et al, 2003

After Effects of Cathodal tDCS: Influence of session duration

Several Factors:

• Sessions: Duration, Number, Interval
• Electrodes: Positions, Size and shape, Number
• Current Intensity
• Brain state: During and Before tDCS
tDCS Effects – Electrodes

Kuo et al, 2013
- HD tDCS stimulates a smaller area, but the resulting change in cortical excitability is dramatically different.
- Used TMS-EMG to assess excitability changes.

Figures adapted from Kuo et al, 2013
What is the effect of tES when applied to non-motor regions?

What are the local and network effects?

What happens during tES?

Choosing tES parameters for treatment?

EEG to Rescue
History

EEG in humans introduced by Hans Berger in 1920s
<table>
<thead>
<tr>
<th>Frequency (Hz)</th>
<th>Phase (Radians)</th>
<th>amplitude (or Power)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10Hz</td>
<td>0</td>
<td>Strength (µV or µV²)</td>
</tr>
<tr>
<td>20Hz</td>
<td>π</td>
<td></td>
</tr>
<tr>
<td>10Hz</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>
Origin

Synaptic activity at the surface of the cortex

EPSP + IPSP

Excitatory pyramidal neurons + inhibitory interneurons
EEG rhythmicity may be caused by synchronization of a pool of neurons engaged in inhibitory processes within the thalamocortical system or feedback loops between and within specific types of excitatory and inhibitory neurons.

References: Whittington, 1995; Whittington, 2000;
Decoding

Different types of computation or level of connectivity

Optimal information processing

References: Bragin 1995; Roopun 2008; Fries 2007
Recording

(1) Spontaneous

(2) Evoked
Time vs. Frequency

Figure adapted from Farzan et al., In revision
EEG Historical Sub bands

**Delta** (1 – 4 Hz)

**Theta** (4 – 8 Hz)

**Alpha** (8 – 13 Hz)

**Beta** (13 – 30 Hz)

**Gamma** (30 – 80 Hz)
Functional role of oscillations

EEG – Behavior Relationship

**Delta (1-4 Hz):** Sleep, learning, motivational processing

**Theta (4-8 Hz):** Memory functions, emotional regulations, processing of new episodic information

**Alpha (8-13 Hz):** May reflect active inhibition of task irrelevant brain areas

**Beta (13-30 Hz):** Divided into slow, medium and high beta sub-bands; Movement execution and control, maintenance of *status quo*

**Gamma (>30 Hz):** Cognitive control, sensory and cognitive processing, perceptual binding

**Comodulation and multiplexing of different frequencies:** Organization of multidimensional information (e.g. sequential items in working memory)

tES May Help Better Understand the Functional Role of Oscillations

Added Value of tES+EEG

1 – Detailed understanding of the tES-induced effect on neural activity in motor and non-motor regions, local and network effects of tES

2 – Discover brain-behavior relationship

3 – Guide the tES input parameters by monitoring brain state

Neuroscience and Clinical Application
Different tES+EEG Approaches

• Offline
  - Record EEG (Rest/+Event)
  - Stop EEG
  - Apply tES
  - Stop tES
  - Record EEG (Rest/+Event)

• Online
  - Record EEG (Rest/+Event)
  - Record EEG & Apply tES
  - Stop tES
  - Record EEG (Rest/+Event)

• EEG-Guided (Online or Offline)
  - Record EEG (Rest/+Event)
  - Apply tES guided by EEG
  - Stop tES
  - Record EEG (Rest/+Event)
System Diagram of tES+EEG Studies

Choose Parameters

<table>
<thead>
<tr>
<th>Input Location</th>
<th>tES Input Parameters</th>
<th>Input Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anatomically guided</td>
<td>Intensity</td>
<td>Guided with respect to a brain state</td>
</tr>
<tr>
<td>Functionally guided</td>
<td>Frequency</td>
<td>Standard Guided</td>
</tr>
<tr>
<td>Scalp landmark Brain atlas MRI, DTI</td>
<td>Standard Guided</td>
<td>Standard EEG Guided</td>
</tr>
</tbody>
</table>

Local/Network Effects

Closed Loop

Feedback

Local/Network Effects

Output Location
- Selected sensors or sources
- All sensors (topography)
- All sources (tomography)

EEG Output Measures

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Mechanisms</th>
</tr>
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<tbody>
<tr>
<td>Amplitude e.g., ERP, GMFA</td>
<td>Local or global excitation/inhibition</td>
</tr>
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<td>Power of each frequency e.g., ERS/ERD</td>
<td>Local or global synchronization</td>
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<tr>
<td>Power as a function of time &amp; frequency e.g., ERSP</td>
<td>Intrinsic properties e.g., Resonant frequency</td>
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<td>Correlation</td>
<td>Functional connectivity e.g., Amplitude, frequency and phase coupling between two or more signals</td>
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<tr>
<td>Coherence</td>
<td>Directed functional connectivity e.g., Information flow</td>
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<td>Synchrony</td>
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<td>Phase-amplitude cross-frequency coupling</td>
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Controlled Brain State

<table>
<thead>
<tr>
<th>Developmental state</th>
<th>Behavioral state</th>
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<tbody>
<tr>
<td>Age</td>
<td>anesthesia, sleep</td>
</tr>
<tr>
<td></td>
<td>wakeful resting</td>
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<td></td>
<td>passive/active sensory processing</td>
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<td>motor movement</td>
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Brain dynamics
- current and history of dynamics
- a preceding stimulus

Disease state
- Disease duration, severity, etc
- Intervention strategies

Output Time
- Relative to input time
- Relative to a brain state
EEG Outcomes: Local Effects

Spontaneous EEG Recording (No Event)

Montage: Anodal tDCS rIFG, cathodal OFC
Resting EEG: Selective decrease of theta band
Behavior: Previously, changes in behavioral inhibition
Clinical Application: ADHD?
EEG Outcomes: Local Effects

EEG + Event

- **Montage:** Anodal tDCS on LDLPFC, cathode on contralateral supraorbital region
- **EEG Rest:** Reduced left frontal delta
- **EEG + Working Memory:** Increased P2 and P3 ERP amplitudes at Fz
- **Performance:** Reduced error rates in working memory
EEG Outcomes: Distant Effects

• Montage: anode L DLPFC / return R Supraorbital vs cathode L DLPFC tDCS
• EEG+ Working Memory: Enhanced performance and amplified ERSP in the theta and alpha bands in posterior leads after anodal vs cathodal tDCS

Figure Adapted from Zaehle et al., 2011
EEG-Guided tES

**Input Location**

| Anatomically guided | Scalp landmark  
|---------------------|------------------|
|                     | Brain atlas  
|                     | MRI, DTI         |
| Functionally guided | fMRI  
|                     | TMS  
|                     | EEG             |

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**Input Time**

Guided with respect to a brain state

**Output Location**

- Selected sensors or sources
- All sensors (topography)
- All sources (tomography)

**EEG Output Measures**

**Analysis**

- Amplitude: e.g., ERP, GMFA
- Power of each frequency: e.g., ERS/ERD
- Power as a function of time & frequency: e.g., ERSP

**Mechanisms**

- Local or global excitation/inhibition
- Local or global synchronization
- Intrinsic properties: e.g., Resonant frequency
- Functional connectivity: e.g., Amplitude, frequency and phase coupling between two or more signals
- Directed functional connectivity: e.g., Information flow

**Controlled Brain State**

- **Developmental state**
  - Age

- **Behavioral state**
  - anesthetia, sleep
  - wakeful resting
  - passive/active sensory processing
  - motor movement
  - cognitive performance

- **Brain dynamics**
  - current and history of dynamics
  - a preceding stimulus

- **Disease state**
  - Disease duration, severity, etc
  - Intervention strategies

**Output Time**

- Relative to input time
- Relative to a brain state
EEG-Guided tES: Location

Faria 2012
EEG evaluation of a patient with continuous spike-wave discharges during slow-wave sleep (CSWS) allowed identification of a spike focus. Cathodal tDCS over the spike focus resulted in a significant decrease in interictal spikes.

Figures Adapted from Faria 2012
EEG-Guided tES: Parameters (e.g., Frequency)

Zaehle et al., 2010

Montage: Posterior tACs at individual alpha oscillations
Resting EEG: Increase in alpha (but not surrounding frequencies) in parieto-central electrodes

Figure Adapted from Zaehle et al., 2012
**EEG-Guided tES: Time**

**Causal relationship between phase and perception**

**Neuling et al., 2012:** Used alpha-tDCS, the timing of the stimuli was arranged relative to the α-tDCS to present the stimuli in specific phase bins.  
**Perception:** Detection thresholds were dependent on the phase of oscillation entrained by alpha tDCS.  
**EEG rest:** Alpha power was enhanced after alpha tDCS

Figures adapted from Neuling et al., 2012
State-Dependency

**Input Location**
- Anatomically guided: Scalp landmark, Brain atlas, MRI, DTI
- Functionally guided: fMRI, TMS, EEG

**tES Input Parameters**
- Intensity: Standard Guided
- Frequency: Standard EEG Guided

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**Output Time**
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Behavioral State: Eyes Open vs. Eyes closed

**Neuling et al, 2013:**
Significant increase in alpha-power after individual-alpha frequency tACS when stimulation was applied with eyes open, but not with eyes closed. Significant increase in alpha coherence with eyes closed, not with eyes open!

Figures adapted from Neuling et al., 2013
Synchronous Stimulation During Task

Fronto-Parietal Theta-Phase Coupling during task

Figures adapted from Polania et al., 2012

Polania et al., 2012
Protocol: 6Hz tACs at 0 or 180 phase difference to frontal and parietal regions during task Performance.
Results: exogenously induced fronto-parietal theta synchronization significantly improved visual memory-matching reaction times; exogenously induced desynchronization significantly worsened task performance
Closed-Loop Studies In Animal

Berenyi et al, 2012: In a rodent model of generalized epilepsy, detection of interictal spikes triggers TES, and aborts the spike-wave discharge bursts.
Other Multimodal Approaches

- Resting EEG, ERP, TMS-EEG**
- fMRI, MRS, NIRS, Combined
Cortical Evoked Potentials

Descending Volleys

Motor Evoked Potentials

Figure Adapted from Farzan F – Neuromethods
Technical Issues (More Work)

Stimulation Artifact in Online Recording is a Challenge

- **tDCS**
  - Easier to clean; a drift that can be eliminated after
  - Some commercially available equipments
  - New technology available that might help in certain circumstances

- **tACS**
  - Within the EEG band of interest; furthermore, changes in impedances may lead to different artifact over time
EEG during tES

Artifact Correction: Standard 3rd order band-pass Butterworth filter (1–250 Hz) eliminated tDCS-induced
Retrieval of EEG during tACS

Helfrich 2014:
**Artifact Correction**: Combination of moving average approach followed by PCA to remove tACS artifact from EEG signal
Added Value of tES+EEG

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Neuroscience and Clinical Application