Neural Engineering term project, spring 2024

Investigating the effect of transcranial electrical stimulation (tES) on tactile acuity via electroencephalography (EEG) and the sensory evoked potential paired pulse depression (SEP-PPD) paradigm

1. Project overview

In this project, you investigate the effect of transcranial direct electrical stimulation (tDCS) on cortical excitability and tactile acuity. The recording protocol consists of the following two sessions:

1.1. Sessions 1 and 2

The protocol is as follows:

i) Tactile acuity performance is assessed via tactile acuity charts.
ii) Resting-state EEG is collected from 32 cortical locations, for 64-64 seconds in eyes open (EO) and eyes closed (EC) state.
iii) Sensory evoked potentials are investigated in the sensory cortex using the SEP-PPD paradigm via stimulating the median nerve of the right arm; 100-100 single and paired (100ms apart) SEPs are evoked.
iv) Resting-state EEG is collected as in ii).
v) tDCS is applied for 20 minutes, either **anodal** or **cathodal**, with stimulating electrodes placed over CP3 and AF8 locations.
vi) Resting-state EEG is collected as in ii).
vii) SEP-PPD is collected as in iii).
viii) Resting-state EEG is collected as in ii)
ix) Tactile acuity performance is assessed via tactile acuity charts as in i).

The protocol for Session 2 is identical to that of Session 1, with the exception of the modality of tDCS in step v): if Session 1 was anodal then Session 2 is cathodal, and vice versa.

2. Hypothesis (high-level)

2.1. **Background**. tDCS is believed to modulate the excitability of neurons by altering their resting membrane potential. In that, cathodal tDCS induces inhibition by driving the resting membrane potential further away from the threshold potential of voltage dependent sodium channels, while anodal tDCS does the opposite, i.e., increase excitability by reducing the resting membrane potential closer to the opening threshold. In turn, tDCS is belieced to have a net effect of altering the regional excitation/inhibition (E/I) ratio (anodal: increase E/I ratio, cathodal: decrease E/I ratio). On the other hand, the SEP-PPD paradigm provides a means to directly test the excitatory/inhibitory tone of the sensory cortex: when evoking two SEPs in quick succession (paired-pulse), amplitude of the second SEP is reduced by response inhibition evoked by the first stimulus. Therefore, anodal tDCS should increase the amplitude of the second SEP (by inducing excitation), while cathodal tDCS should further decrease it (by inducing further inhibition).

Finally, it has been suggested that excitatory tES might improve tactile acuity performance; however, a causal relationship between excitation/inhibition balance in the sensory cortex and tactile acuity has not been explicitly confirmed yet.

2.2. **Hypothesis:** In this study, we hypothesize, that sensory performance is dependent on the E/I balance in the primary sensory cortex. To confirm this, we investigate if anodal/cathodal tDCS has a positive/negative effect on tactile acuity performance, and we use the SEP-PPD paradigm to link this effect (or lack thereof) to the E/I ratio of the sensory cortex. In other terms, we utilize the SEP-PPD paradigm to confirm the induced excitatory/inhibitory effect of anodal/cathodal tDCS itself, and tactile acuity charts to assess sensory performance. Note that since feedback was not provided on tactile acuity performance during the study, we do not expect substantial practice effects (that would bias the performance outcomes).

3. Objectives

3.1. Investigate effect of tDCS on tactile acuity performance: do anodal and cathodal tDCS have opposite effects on tactile acuity? What is the performance threshold (i.e., a difficulty level where tactile acuity begins to drop), and does tDCS have an effect of this sensory threshold?

3.2. Analyze EEG activity to show the neurophysiological effects of anodal and cathodal tDCS (i.e., analyze both sessions independently):

3.2.1. SEP-PPD: Compute the grand average (both pre- and post-tDCS) SEP for single pulses, paired-pulses, and the difference between the two (paired minus single pulses) over the contralateral sensory cortex (ideally, CP5 region).

3.2.2. **Optional assignment 1:** Resting-state EEG: compare pre- and post-tDCS neural markers of excitatory/inhibitory tone. Are there resting-state EEG markers that capture the excitatory/inhibitory effect of anodal/cathodal tDCS? Such possible neural markers include broadband spectral slope (use e.g., FOOOF or IRASA techniques, see literature) or resting alpha (8-13 Hz) band-limited power.

3.3. Based on what you conclude from 3.1 and 3.2, can the original hypothesis be confirmed, i.e., can sensory performance be linked to E/I balance in the sensory cortex?

3.4. **Machine learning objective**: Although single and paired SEPs are easy to distinguish on grand average plots, detecting them on a single-trial basis is more difficult. You will test if this discrimination is affected by anodal and cathodal tDCS. In that, the pre-tDCS data of the two sessions can be considered identical, and thus they can be pooled to train a classifier that distinguishes between single and paired SEPs (Note: the datasets from the two sessions will contain *between-session non-stationarities*; try to find a way to eliminate them as much as possible). The expected performance of this decoder can be evaluated by k-fold cross-validation. Then, this decoder can be tested on the two post-tDCS datasets independently. What do you expect in terms of classification performance, i.e., will it increase/decrease/not change on the anodal and the cathodal post-tDCS datasets?

4. Data description

Data will be provided for both sessions. This includes:

4.1. Resting-state EEG: 1. pre-tDCS pre-FES; 2. pre-tDCS post-FES; 3. post-tDCS pre-FES and 4. post-tDCS post-FES. Every EEG recording contains 64 seconds of EO and 64-seconds of EC data (indicated by markers, see below). From both conditions, a sample of shorter epochs (e.g., of length 8 seconds) should be selected for analysis (e.g., 5 epochs of length 8 seconds, they can overlap to some extent).

4.2. SEP-PPD data: 1. pre-tDCS and 2. post-tDCS (each in two runs, which can be pooled). Both datasets (pre- and post-tDCS) contain 100-100 single-pulse and paired-pulse SEPs. The position of the sensory stimulus in case of single-pulse, and the position of the first stimulus in case of paired-pulse are denoted by markers (t=0). The time-period of interest is roughly from t=-0.1s to t=0.6s. Isolate trials for analysis.

4.3. Tactile acuity performance: 1. pre-tDCS and 2. post-tDCS (each in two runs, which can be pooled). Performance will be provided separately for the 9 difficulty levels.

5. Data structure

Data is organized the following way. All data (per participant) will be sorted into two folders: **Session_Anodal** and **Session_Cathodal**. Within these, the data structuring will be the same (see below). Note that the .gdf files are organized in the following manner: the first 32 columns contain data for the 32 EEG channels, and the last channel contains the trigger values (markers for events). There will be an additional number of channels (e.g., columns 33-37) that only contain noise (these are for optional bipolar channel data such as EOG or EMG, which we did not record in these sessions).

5.1. Resting-state EEG: four .gdf files (Subject_***_Session_***_RS subfolder).

5.1.1. Subject_***_RS_s***_r1_<date>.gdf: pre-tDCS, pre-FES data
5.1.2. Subject_***_RS_s***_r2_<date>.gdf: pre-tDCS, post-FES data
5.1.3. Subject_***_RS_s***_r3_<date>.gdf: post-tDCS, pre-FES data
5.1.4. Subject_***_RS_s***_r4_<date>.gdf: post-tDCS, post-FES data

In these .gdf files, the last channel (column) is the trigger channel, containing markers for specific events:

- 20: start of **Eyes open** recording
- 30: end of **Eyes open** recording (64 seconds in length)
- 40: start of **Eyes closed** recording
- 50: end of **Eyes closed** recording (64 seconds in length)

Hint for analysis: use clean (i.e., artifact-free) segments of length 4 or 8 seconds for analysis, exclude epochs with huge amplitude absolute values (e.g., abs(EEG) > 100 μV), exclude channels T7, T8, M1 and M2.

5.2. **SEP-PPD data:** four .gdf files (Subject_***_Session_***_SEP_PPD subfolder).

- **5.2.1.** Subject_***_SEP_PPD_s***_r1_<date>.gdf: pre-tDCS, first run
- **5.2.2.** Subject_***_SEP_PPD_s***_r2_<date>.gdf: pre-tDCS, second run
- **5.2.3.** Subject_***_SEP_PPD_s***_r1_<date>.gdf: post-tDCS, first run
- **5.2.4.** Subject_***_SEP_PPD_s***_r2_<date>.gdf: post-tDCS, second run

All of these .gdf files contain 50-50 single and paired-pulse SEPs, totaling to 100-100 each for both pre- and post-tDCS. The last channel is again the trigger channel, containing markers for specific events:

- 101: **FES pulse in single-pulse trial** (evoking single SEP)
- 102: **first FES pulse in paired-pulse trial** (evoking paired SEP)

Hint for analysis: isolate single- and paired-pulse trials with some buffer (e.g., if position of trigger 101 is t_0=0, then isolate from t_{start}=-0.1s to t_{end}=+1s), exclude trials with blinks or other artifacts (EEG amplitude too large). FES was applied to the right median nerve, so SEPs should be looked for in the contralateral primary sensory cortex.

5.3. **Behavioral data:** In tabular format for both sessions (anodal and cathodal tDCS). There were 9 difficulty levels, denoted by 0.3 (easiest difficulty, top row on TA charts), decreasing in steps of 0.1 until -0.5 (most difficult condition, bottom row on TA charts). For each condition, pre- and post-tDCS performance will be provided as an integer ranging between 0 and 1, denoting the proportion of correct responses for the given difficulty level.

6. Literature

You might find the following articles helpful:

- Saito, K., Otsuru, N., Inukai, Y., Miyaguchi, S., Yokota, H., Kojima, S., Sasaki, R. and Onishi, H., 2019. Comparison of transcranial electrical stimulation regimens for effects on inhibitory circuit activity in primary somatosensory cortex and tactile spatial discrimination performance. *Behavioural brain research*, *375*, p.112168.

- Saito, K., Otsuru, N., Inukai, Y., Miyaguchi, S., Yokota, H., Kojima, S., Sasaki, R. and Onishi, H., 2019. Comparison of transcranial electrical stimulation regimens for effects on inhibitory circuit activity in primary somatosensory cortex and tactile spatial discrimination performance. *Behavioural brain research*, *375*, p.112168.

- Krause, B., Márquez-Ruiz, J. and Kadosh, R.C., 2013. The effect of transcranial direct current stimulation: a role for cortical excitation/inhibition balance? *Frontiers in human neuroscience*, *7*, p.602.
- Cecotti, H. and Ries, A.J., 2017. Best practice for single-trial detection of event-related potentials: Application to brain-computer interfaces. *International Journal of Psychophysiology*, *111*, pp.156-169.

Optional:

- Gao, R., Peterson, E.J. and Voytek, B., 2017. Inferring synaptic excitation/inhibition balance from field potentials. *Neuroimage*, *158*, pp.70-78.
- Donoghue, T., Haller, M., Peterson, E.J., Varma, P., Sebastian, P., Gao, R., Noto, T., Lara, A.H., Wallis, J.D., Knight, R.T. and Shestyuk, A., 2020. Parameterizing neural power spectra into periodic and aperiodic components. *Nature neuroscience*, *23*(12), pp.1655-1665.