Investigating the effect of transcranial electrical stimulation on tactile acuity via electroencephalography and the sensory evoked potential paired pulse depression paradigm

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Abstract

Transcranial electrical stimulation (tES) plays an important role in cortical excitability. The one-way flow of current in transcranial direct current stimulation (tDCS) reliably modulates sensory-evoked potentials (SEP), making it versatile for investigating tactile perception when applied over the primary somatosensory region [1]. In this study, tDCS was applied to investigate the varying effects of cathodal and anodal stimulation on tactile acuity using electroencephalogram (EEG) recordings and the sensory-evoked potential paired-pulse paradigm (SEP-PPD). Behavioral analyses reveal consistent tactile performance enhancements post-tDCS, with no significant change in sensory threshold. Neurophysiological analyses demonstrate minor changes in SEP waveforms following anodal and cathodal tES, with no significant alterations in SEP-PPD biomarkers. Classification exhibits high accuracy in distinguishing single and paired pulses in both pre-and post-tES conditions.

1. Introduction

Tactile perception is a fundamental aspect of human sensory experience, crucial for interacting with the environment. Tactility is a sensory modality that relays information to the brain such as the internal feeling when touching an object, as well as the texture, shape, and orientation of the object itself. The primary site of tactile processing in the brain is the primary somatosensory cortex (S1), where incoming tactile information is initially received and processed.

Literature has demonstrated that tES interventions, including tDCS, exerts modulatory effects on neuronal excitability, manifesting in the form of regional excitation (E) and inhibition (I). In fact, research suggests that tES over the S1 region can improve tactile perception. Tactile activities, such as a grating orientation task (GOT) have shown increased performance as a result of tES intervention. These changes are evidenced by changes in the SEP-PPD paradigm [2]. SEP-PPD reflects the attenuation or amplification of SEPs in response to paired stimuli. Specifically, anodal and cathodal tDCS interventions lead to changes in SEP-PPD over the S1, an observation suggesting alterations to the E/I ratio [2]. This phenomenon is likely attributable to increased neuronal activity or enhanced synaptic plasticity.

It is hypothesized that tactile acuity performance relies on the balance between excitatory and inhibitory activity in S1. The impact of anodal and cathodal tDCS on tactile acuity is explored using both the SEP-PPD paradigm to validate the E/I influence of tDCS and the tactile acuity assessments to measure sensory performance. Notably, participants did not receive feedback during the tactile acuity assessments, thus practice effects are not expected to skew results.

2. Methods

2.1 Subject Overview

The experiment recruited 12 individuals, including both male and female subjects. Age specifications, hand dominance, and brain conditions were not provided. All subjects provided written consent to participate in the study.

2.2 Experimental Protocol

Experimentation was conducted across two sessions per subject, including a consistently structured recording protocol. Figure 1 provides both the chronological and temporal workflow of the recording protocol.

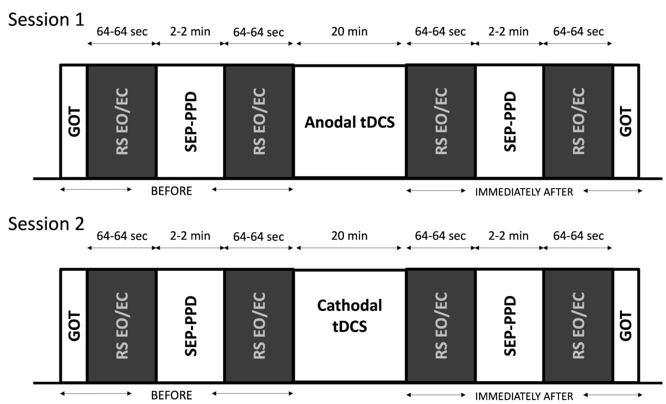

Figure 1. Schematic of experiment across two sessions. In Sessions 1 and 2, all subjects underwent a series of GOTs, resting state EEG recordings (eyes-open and eyes-closed), FES right median nerve stimulation, and resting state EEG recordings prior to randomized tDCS protocol. All subjects would undergo the reversed procedure after the tDCS protocol. Durations and orientation with respect to tDCS are shown. Note: Session 1 and Session 2 are not assigned to Anodal t-DCS and Cathodal t-DCS, respectively, but rather, randomized on a subject-wise basis.

2.3 Behavioral Objectives

For behavioral analysis, a paired-t test was used on the tactile acuity data obtained from GOTs. Comparisons were made across the pre- and post- tDCS data, as well as performance overtime from pre- to post- tDCS. The effects of cathodal and anodal stimulation on performance were investigated by plotting the accuracy trend against difficulty level. Patterns in the subject-level data were analyzed by calculated performance mean and variance to investigate if the post-stimulation effect has changed the performance threshold (difficulty of which accuracy starts to drop).

2.4 Neurophysiological Objectives

Prior to conducting the analysis of the SEP-PPD paradigm, noise reduction was necessary. In order to reduce noise, a zero-phase 4th-order Butterworth bandpass filter was used across the range of 1-50 Hz. Implications of 4th-order filtering balance group delay, computational complexity, and temporal filtering for physiological signals. The frequency range was established through visual examination of Welch's power spectral density plot, employing eight windows with a 50% overlap. This determination also took into account the inherent presence of fast components within the SEP.

Noisy channels M1, M2, T7, and T8 were removed in addition to performing mean subtraction to achieve a baseline correction in the EEG signal. The filtered and normalized data was segmented into epochs. Each SEP-PPD recording contained 50 epochs for both single and paired pulse from -0.1s - +1s from stimulation. Resting data was separated into 8 epochs for each recording session of duration 8s. Spatial filtering was performed on the epochs to eliminate poor signal quality and signals with amplitude > ±100uV were eliminated as well. Grand averages were extracted from the remaining epochs and used for statistical analysis. Particularly, the interesting grand average plot averages across various channels in the S1 region.

Analysis of the SEP-PPD signal behavior was conducted using the N20 and P25 peaks, identified through visual inspection of the grand average plots and validated through a peak finding algorithm. The N20 and P25 values were extracted directly from the SEP waveform, and the N20 SEP-PPD, P25 SEP-PPD, and N20/P25_SEP-PPD responses were measured as the ratio of the second SEP pulse to the first SEP pulse. N20/P25_SEP-PPD is E/I balance.

2.5 Classification Objectives

The initial classification analysis for SEP waveforms primarily focused on extracting time-domain features, as the specific event-related potentials (ERP) occurred via modulation in the time domain. Thus, features such as Mean Absolute Value (MAV), N20_P25 Peak Amplitude (pk2pk), and Slope Sign Change (SSC), were chosen to capture distinctions in the temporal signal. In addition, power spectral density features, a measure of power in the frequency domain, were extracted for the sake of feature robustness. Feature selection was performed using the minimum-redundancy maximum relevance (mRMR) algorithm, which tends towards features with high class-correlation and low self-correlation. Particularly focusing on the somatosensory cortex, channels surrounding the

Cp5 location were of high interest, and they were thus targeted for feature extraction.

The selected models include the following: linear support vector machine (ℓ-SVM), k-nearest neighbors (KNN), and linear regression (LR). SVM classifiers have been shown to detect ERP with high accuracy on a single-trial basis [3]. The models were trained per subject on all respective pre-tDCS data and tested separately on the post-anodal tDCS and post-cathodal tDCS data. The training and testing splits among the respective datasets were implemented using a 5-fold cross validation approach. Evaluation of the models was carried out in two ways. First, the mean accuracy output was calculated across the folds for each model. Secondly, the area under the curve (AUC) was calculated on the receiver operating characteristic (ROC) curve.

2.6 Statistical analysis

To ensure statistical analysis was appropriate, a Lilliefors normality test was conducted to determine the distribution of the data at hand. This was a necessary step for all statistical analysis. Should any variable in a set of grouped variables have found an irregular distribution, the statistical comparison was carried out using the Wilcoxon signed-rank test. Otherwise, comparisons were made using a paired t-test.

3. Results

3.1 Behavioral outcome relative to tDCS.

Subjects observe similar improvement in their tactile performance after both anodal and cathodal tDCS, shown in Figure 2. The average performance threshold for accuracy to drop is after the difficulty level of 0.

The anodal and cathodal data distribution were plotted separately by subject with variance bars, in Figure 3. Variations were observed across subjects, although the improvement effects for both tDCS types were generally consistent. When examining at the individual level, the variance stemmed from an individual's baseline level of acuity performance. Post-stimulation performance aligned with the subject baseline, showing similar percentile improvements across all subjects. However, only one subject experienced a performance threshold increase of 1 level after tDCS, which may be attributed to random performance variation, possibly due to guessing.

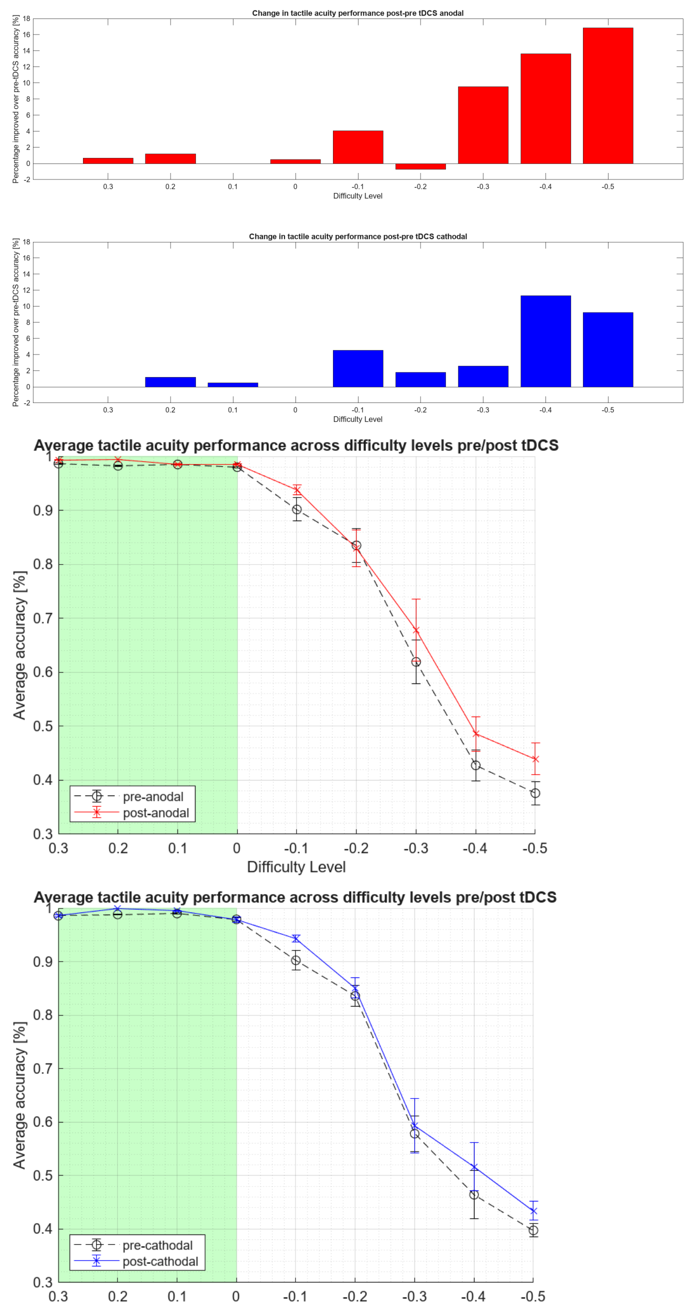

Figure 2. Average Tactile Acuity Performance Across Difficulty Levels pre/post-tDCS. Anodal (red). Cathodal

tDCS (blue). Difficulty level threshold (green). Pre-tDCS (dashed). Post-tDCS (solid).

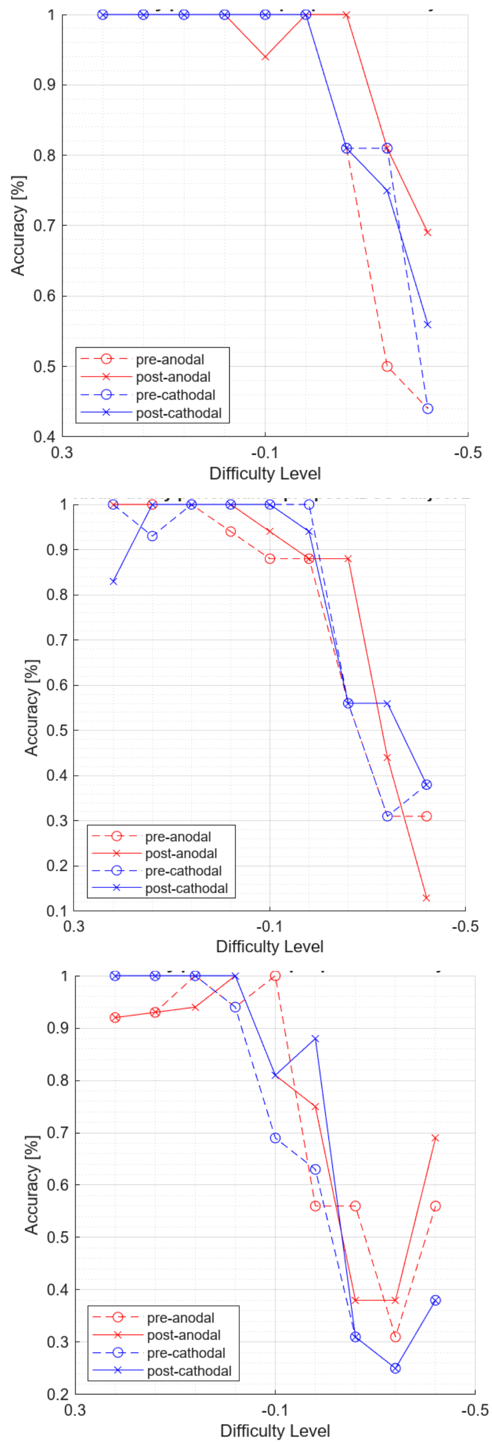

Figure 3. Tactile Acuity Performance Pre/Post-tDCS, Subjects 1, 2, and 3.

3.2 Effects of cathodal vs. anodal t-DCS on SEP waveforms and SEP-PPD biomarkers.

Figure 4 displays the grand average of somatosensory evoked potentials averaged across six channels in S1 for Subject 1. The waveforms, induced by single and paired-pulse FES stimulation at the right median nerve, are displayed in each the anodal and cathodal t-DCS condition.

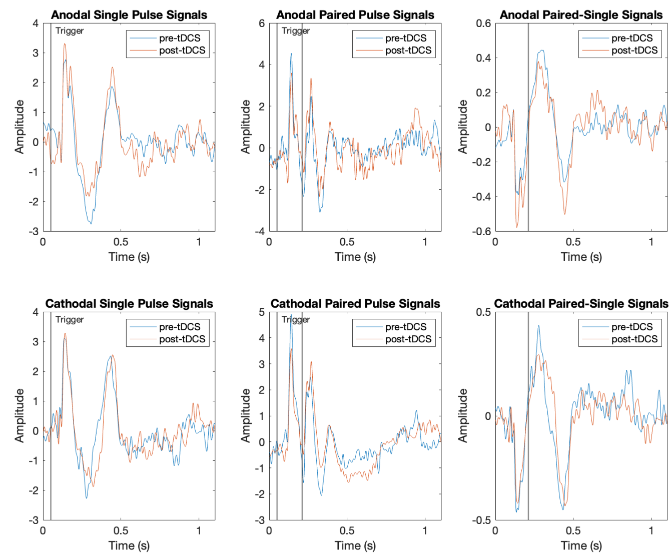

Figure 4. Subject 1, Grand Average Plots for Anodal vs. Cathodal tDCS. Grand averaged single and paired-pulse SEP waveforms averaged across CP5, CP1, C3, P7, P3, FC5 channels in the somatosensory cortex. Pre-tDCS (blue line) represents the waveform captured immediately before tDCS stimulation. Post-tDCS (orange line) represents the waveform captured immediately after tDCS stimulation. Trigger (black xline) represents the time point at which FES stimulation occurred at the right median nerve (single: ~0.05s, paired: ~0.20s).

Subject	R	P
101	0.87463	0.12537
102	0.78912	0.21088
103	-0.233	0.766
101 & 102	0.75466	0.03
All	0.073	0.821

Table 1. Tactile Performance and E/I balance. SubjectID; Correlation coefficient; p-value. E/I balance was calculated using the ratio of peak-to-peak voltage in N20/P25 SEP PPD. An additional test was performed with 101 and 102 because 103 contained too many outliers to extract relevant information.

Changes in SEP-PPD are most evident in the first peak's amplitude as well as the second peak's amplitude. To examine these changes, the effect of tDCS on the first and second N20 and P25 responses were analyzed. Figure 5 shows the results of this analysis. Amplitudes between N20 and P25 were measured as well as N20 and P25 individually. The ratios were determined by dividing the amplitude of the second pulse to the first pulse. Thus the ratio is affected by changes in both components of the waveform.

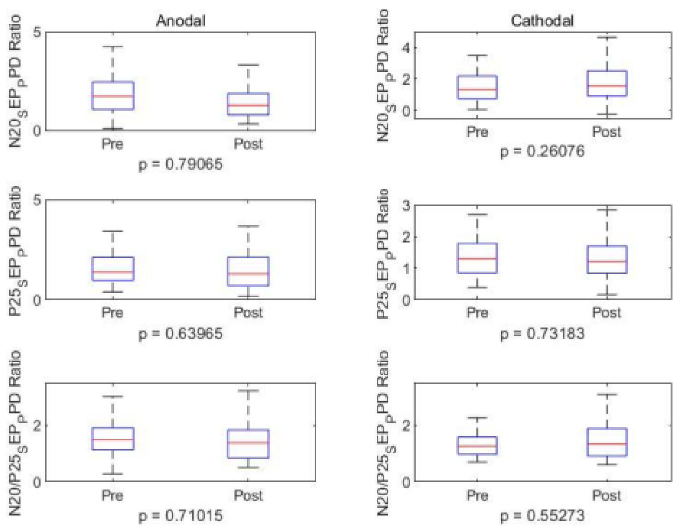

Figure 5. Effect of tDCS on N20SEP_PPD (upper), P25_SEP_PPD (middle), and N20/P25_SEP_PPD. There is no significant difference between pre and post-tDCS on SEP_PPD. Anodal stimulation resulted in a minor decrease in both N20_SEP_PPD and P25_SEP_PPD while cathodal displayed a slight increase in N20_SEP_PPD.

3.3 Trial-wise classification of single/paired pulse SEP waveforms before and after cathodal and anodal tDCS.

The minimum redundancy maximum relevance algorithm selected for the top six features across each channel, aiming for dimensionality reduction. The top feature, MAV, has an mRMR score of 0.54625 from channel CP5. The remaining five ranked features have values of 0.44909, 0.33629, 0.33566, 0.31786, and 0.28797, respectively. These features, from corresponding channels, were targeted for classification.

The classification accuracy of three different models was tested: ℓ-SVM, KNN, and LR. Table 1 shows the average performance of the three models, given the regimen of tDCS (as pre or post, and as anodal or cathodal).

	SVM	KNN	LR
Pre - Anode	0.96 $\pm$0.0579	0.87778 $\pm$0.0894	0.9568 $\pm$0.0338
Post - Anode	0.96 $\pm$0.0579	0.60667 $\pm$0.0983	0.93152 $\pm$0.0215
Pre - Cathode	0.95778 $\pm$0.0579	0.85556 $\pm$0.1673	0.95614 $\pm$0.0222
Post - Cathode	0.95556 $\pm$0.0579	0.73111 $\pm$0.1151	0.93495 $\pm$0.0242

Table 1. Classification Accuracy for pre- and post- tDCS regimens. Mean accuracy ± standard deviation.

Average classification accuracy is suitable for datasets with balanced classes, thus the epoch rejection ratio of single-pulse and paired-pulse classes were tested. Single-pulse epochs experienced a near significant rejection rate ($p \approx 0.05$) when compared to paired-pulse epochs. To ensure the robustness of classification metrics, the AUC of the ROC for each model was calculated. LR observed AUC = 1.0000 for Post-Anode and Post-Cathode, supporting the consistently high performance represented by the average accuracy. ℓ-SVM showed an AUC = 0.8933 for Post-Anode and 0.9571 for Post-Cathode, which is expected according to the average accuracy values. Lastly, KNN saw a similarly poor AUC, equal to 0.6050 and 0.6860 respectively to Post-Anode and Post-Cathode.

Statistical comparison was conducted among varying combinations of the classification process, captured by Figure 6. According to Figure 6.1, no model observes statistically different single/paired-pulse classification accuracies between pre- and post- anodal tDCS stimulation ($p > \alpha = 0.05$). Similarly, ℓ-SVM and KNN observe no statistical significance between their respective pre- and -post cathodal tDCS classification accuracies ($p > 0.05$). Only LR shows significant difference in performance between pre- and post- tDCS, and the accuracy values are large, [0.91475, 0.97836].

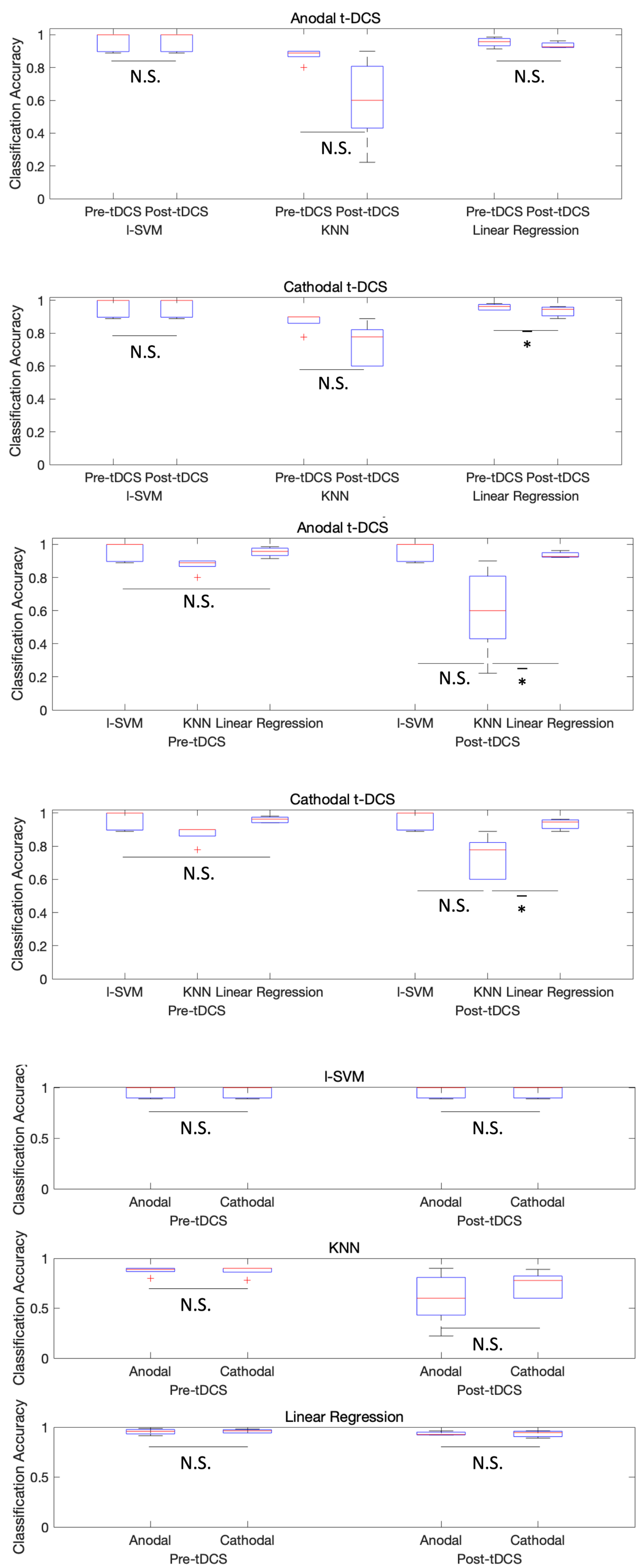

Figure 6. Effects of Pre/Post t-DCS, Anodal/Cathodal-tDCS, Classification Model, Single vs. Paired Accuracy. Interquartile range (blue); Median (red); *6.1* The LR model shows statistically significant classification accuracies between the pre-tDCS and post-tDCS stimulation for cathodal tDCS ($p < 0.05$). *6.2* The KNN and LR models observe a significant difference in accuracy for both post-anodal and post-cathodal tDCS ($p < 0.05$). *6.3* Grouping anodal and cathodal t-DCS according to pre-tDCS and post-tDCS for each model type yields no statistically significant differences in classification accuracy. *Note: 'N.S.' labels indicate 'Not Significant'; '*' labels indicate $p < 0.05$.*

Neither pre-anodal nor pre-cathodal tDCS yields statistical significance when differentiating between classification accuracies among model types in Figure 6.2 ($p > 0.05$). Post-anodal and cathodal tDCS shows statistical differences in accuracy between KNN and LR models ($p < 0.05$), though, none between ℓ-SVM and KNN model accuracies ($p > 0.05$). Figure 6.3 indicates that there are no significant differences between anodal and cathodal tDCS within each model ($p > 0.05$).

4. Discussion

The study did not reveal significant discrepancies in tactile acuity between anodal and cathodal tDCS. However, both types of stimulation demonstrated an improvement in tactile performance before and after the stimulation. Additionally, notable alterations were observed in the excitation/inhibition balance following tDCS.

The initial hypothesis was validated: there is a discernible correlation between brain excitability and tactile perception. The heightened excitability induced by anodal tDCS appears to enhance the ability to discern tactile details. This reinforces the research that tDCS can modulate cortical activity, consequently influencing our tactile experiences.

This study did not reveal significant differences in tactile acuity between anodal and cathodal tDCS, as both polarities exhibited improved performance before and after the intervention. The consistent enhancement in tactile acuity regardless of polarity demonstrates the robustness of tDCS in modulating tactile perception. Ultimately, while the findings support the hypothesis, the complex interaction between the E/I balance and tDCS suggests the need for further research and analysis.

5. Appendix

References

[1] T. Reed and R. Cohen Kadosh, "Transcranial electrical stimulation (tES) mechanisms and its effects on cortical excitability and connectivity," Journal of Inherited Metabolic Disease, vol. 41, no. 6, pp. 1123–1130, 2018, doi: https://doi.org/10.1007/s10545-018-0181-4.

[2] K. Saito et al., "Comparison of transcranial electrical stimulation regimens for effects on inhibitory circuit activity in primary somatosensory cortex and tactile spatial discrimination performance," Behavioural Brain Research, vol. 375, p. 112168, Dec. 2019, doi: https://doi.org/10.1016/j.bbr.2019.112168.

[3] H. Cecotti and A. J. Ries, "Best practice for single-trial detection of event-related potentials: Application to brain-computer interfaces," International Journal of Psychophysiology, vol. 111, pp. 156–169, Jan. 2017, doi: https://doi.org/10.1016/j.ijpsycho.2016.07.500.

Statement of Work

Objectives / Work	**Holland Ernst (%)**	**Yue Jiang (%)**	**Spencer Shisler (%)**
Behavioral	0	100	0
Neurophysiological Analysis	30	0	70
Correlation	20	0	80
Machine Learning	85	5	10
Presentation	33	33	33
Proposal	45	10	45
Report	60	20	20