A Novel Synchronized Stimulation Method to Improve the Tactile Localization Ability of Post-Stroke Patients

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Abstract

Background

Transcranial direct-current stimulation (tDCS) has shown promise in enhancing neural plasticity and functional abilities in post-stroke patients. However, determining the optimal protocol for this method remains an open question. Our study proposes a novel approach: synchronized stimulation that combines mechanical and electrical stimuli. We hypothesize that this approach will enhance tactile localization ability in post-stroke patients.

Methods

We recruited a total of 23 patients and conducted four different types of experiments involving periodic mechanical stimulation on their fingertips. The primary objective was to assess the participants' ability to accurately localize the location of the mechanical stimulation. In one experiment, only mechanical stimulation was administered. In the remaining three experiments, electrical stimulations were combined with the mechanical stimulation. The electrical stimulations comprised of one of the following protocols: (1) tDCS pulses administered solely for the initial five seconds of the session, (2) continuous tDCS pulses throughout the entire duration of the mechanical stimulation, and (3) tDCS pulses synchronized precisely with the timing of the mechanical stimulation.

Results

A noteworthy enhancement in tactile localization ability was observed when the electrical and mechanical stimulations were synchronized.

Conclusion

Our findings demonstrate that the integration of electrical brain stimulations with simultaneous mechanical stimulation of the fingertips resulted in enhanced neural activities. This synchronized integration holds the potential to improve perception and may serve as a vital approach in the treatment of post-stroke patients.

1. Introduction

Patients who have suffered a stroke often experience a range of impairments that severely affect their day-to-day functioning [1]. Among the challenges faced by post-stroke individuals are unilateral motor weakness, limb hemiparesis, spasticity, and coordination difficulties, which lead to a significant decline in motor abilities [1]. Restoring motor function following a stroke is a complex task due to pathophysiological and clinical factors [2]. Various forms of stimulation, including electrical stimulation,
have emerged as effective approaches in post-stroke rehabilitation [3, 4]. Electrical stimulation techniques, such as neuromodulator non-invasive brain stimulation (NIBS) with transcranial direct-current stimulation (tDCS), have gained attention as experimental therapies for promoting motor recovery after a stroke [5]. The application of tDCS in post-stroke motor recovery was introduced in 2005 and has since been widely utilized [6, 7, and 8]. Recent advancements, such as the closed-loop EEG-tDCS method, have shown promising applications in this field [9]. Furthermore, novel approaches like multichannel network-based tDCS, particularly employing a 5-channel tDCS scheme, have demonstrated improved efficacy in healthy subjects, suggesting potential benefits for future stroke rehabilitation cases [10].

In addition to motor deficits, post-stroke patients often experience impairments in their tactile abilities, including reduced touch detection and localization. Some individuals with focal brain lesions may exhibit tactile detection capability, but they struggle with accurately localizing tactile stimuli on the skin surface. The process of perceiving the location of touch involves intricate neural mechanisms. When an object is touched, signals from touch receptors and proprioceptors in the muscles are transmitted via neurons to the dorsal horn of the spinal cord. From there, the signals are relayed through the spinal cord to reach the thalamus and subsequently the primary somatosensory cortex (S1 region) [11, 12]. Recent studies propose that conscious detection plays a crucial role in the localization of tactile stimuli [13], although there are contrasting findings [14, 15, 16], and the underlying mechanism of tactile localization remains poorly understood.

This research focuses on enhancing the localization ability of stroke patients, as poor tactile abilities are commonly addressed through mechanical stimulation in the form of physical therapy. However, electrical stimulation has also demonstrated effectiveness in improving tactile function in post-stroke cases. Recently, simultaneous mechanical and electrical stimulation has gained attention as a potential intervention for stroke patients [17]. Previous studies have reported noticeable improvements in the motor abilities of stroke patients when electrical stimulation is synchronized with rehabilitation movement frequency [17, 18]. In this study, we applied simultaneous mechanical and electrical stimulations to a group of stroke patients and observed a significant improvement in their tactile localization performance. Furthermore, we hypothesized that synchronizing these two types of stimulations would yield even greater effectiveness. To validate this hypothesis, we compared the localization abilities of patients across different experimental conditions. The experiment involving synchronized stimulation showed a remarkable enhancement in tactile ability compared to the other experimental setups.

2. Methods

2.1. Participants

This study involved the participation of 23 patients who had experienced a stroke within the past 2 to 6 months and were between the ages of 25 and 75. Ethical approval was obtained from the Iran Medical Ethics Committee, and all patients provided informed consent to be part of the study.
All participants exhibited a low level of tactile localization ability in either the right or left half of their bodies, to the extent that they had difficulty localizing any mechanical stimulation applied to their fingertips on the affected body side. However, they were capable of detecting the presence of these stimulations. The patients also agreed not to receive any medication or physical therapy during the course of the experiment.

### 2.2. Experimental protocol, Intervention

The experimental protocol consisted of four experiments conducted on a group of 23 patients, with each experiment performed within a 24-hour time frame. For patients with deficiency in their right half of the body, cathode and anodal and electrodes were connected to the S1-left and S1-right regions of their brains, respectively. For patients with deficiency in their left half of the body, the electrodes were connected in the reverse manner.

In the first experiment, referred to as the tDCS-sham stimulation, the group received tDCS sham pulses [9]. A 2.5mA current was applied for only 5 seconds, simultaneously with intensive mechanical stimulations applied to their fingertips (the first and fourth stimulations in Fig. 1). To perform the mechanical stimulation, each finger was stimulated approximately 10 times within a 5-second interval, with 20-second intervals between the stimulations. During these 20-second intervals, the patients were instructed to localize the preceding stimulation, and their responses were recorded. Each individual received a total of 50 mechanical stimulations, with the sequence of fingertip stimulations selected randomly from a uniform distribution for each trial. The performance of each patient was measured as the correct localization percentage.

In the second experiment, similar to the first, tDCS stimulation was applied, but with a steady 2.5mA electrical current (the first and third stimulations in Fig. 1).

In the third experiment, the same protocol as the second experiment was followed, with the only difference being that the 2.5mA current was applied only during the application of physical stimulation. The electrical current was disconnected between each set of two mechanical stimulations, thereby synchronizing the electrical stimulation with the mechanical stimulation (the first and second stimulations in Fig. 1). This experimental setup was referred to as tDCS-sync stimulation.

Finally, in the fourth experiment, the same mechanical stimulations were applied without any tDCS stimulation, and the results were recorded. This experiment served as the control condition and was referred to as the No-tDCS stimulation. The subjects were completely blind to the types of stimulations being administered.

### 2.3. Statistical analysis

All experiments were conducted on each participant, resulting in paired data for analysis. To investigate the impact of electrical stimulation on correct localization, the effect was compared across four groups: No-tDCS, tDCS-sham, tDCS, and tDCS-sync. In order to demonstrate that the effect of tDCS-sync was
superior to the other stimulations, pairwise comparisons were performed between the four groups using Wilcoxon signed-rank tests. The correct localization (CL) distributions were found to pass the normality test, indicating that normal distributions could be assumed for CL values in different experiments.

To examine potential differences in mean CL responses among the different experiments, a repeated measure analysis of variance (ANOVA) was conducted. Post-hoc analysis with Bonferroni correction was applied to compare the means of CL values between different experiments in pairwise comparisons [19]. Additionally, the Friedman test, a non-parametric test, was used to test the hypothesis. All statistical analyses were performed using MATLAB version 2021 and SPSS software version 22.0.

3. Results

To evaluate the impact of the proposed stimulation method on improving tactile localization ability in patients, we measured the percentage of correct localization (CL) in each experiment. We compared the CL distributions among four different stimulation schemes. The average CL without any electrical stimulation was approximately 25% (mean ± SEM, 0.257 ± 0.033, Fig. 2 & Table 1). Similarly, the CL in the tDCS-sham stimulation was around 24% (mean ± SEM, 0.240 ± 0.034, Fig. 2 & Table 1). There was no significant difference in CL between tDCS-sham and No-tDCS stimulations (mean ± SEM, ∆CL No-tDCS & tDCS-sham = 0.017 ± 0.011, Wilcoxon signed-rank test, P No-tDCS & tDCS-sham = 0.855, Fig. 3F).

Table 1
The mean, standard error of mean and 95% confidence interval of CL in four experiments.

<table>
<thead>
<tr>
<th>Group name</th>
<th>Mean</th>
<th>Std. Error</th>
<th>95% Confidence Interval</th>
<th>Lower Bound</th>
<th>Upper Bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>No-tDCS</td>
<td>0.257</td>
<td>0.033</td>
<td>0.188</td>
<td>0.327</td>
<td></td>
</tr>
<tr>
<td>tDCS-sham</td>
<td>0.240</td>
<td>0.034</td>
<td>0.171</td>
<td>0.310</td>
<td></td>
</tr>
<tr>
<td>tDCS</td>
<td>0.265</td>
<td>0.032</td>
<td>0.199</td>
<td>0.332</td>
<td></td>
</tr>
<tr>
<td>tDCS-sync</td>
<td>0.365</td>
<td>0.030</td>
<td>0.303</td>
<td>0.428</td>
<td></td>
</tr>
</tbody>
</table>

The CL increased to 26% in the tDCS stimulation (mean ± SEM, 0.265 ± 0.032, Fig. 2 & Table 1). Although there was a clear trend of improvement with tDCS, it did not reach significance compared to No-tDCS, but it was significantly higher than tDCS-sham stimulation (mean ± SEM, ∆CL tDCS_No-tDCS = 0.008 ± 0.010, Wilcoxon signed-rank test, P tDCS_No-tDCS = 1.000; mean ± SEM, ∆CL tDCS_tDCS-sham = 0.024 ± 0.012, Wilcoxon signed-rank test, P tDCS_tDCS-sham = 0.0306, Fig. 3B&D).

The CL significantly increased to 36% in the tDCS-sync stimulation (mean ± SEM, 0.365 ± 0.030, Fig. 2 & Table 1), representing a 44% increase compared to No-tDCS stimulation. There was a significant difference between CL in the tDCS-sync stimulation and both No-tDCS and tDCS-sham stimulations (mean ± SEM, ∆CL tDCS-sync_Without-tDCS = 0.108 ± 0.022, Wilcoxon signed-rank test, P tDCS-
sync_Without-tDCS = 0.000; mean ± SEM, Δ CL tDCS-sync_tDCS-sham = 0.124 ± 0.022, Wilcoxon signed-rank test, P tDCS-sync_tDCS-sham = 0.000, Fig. 3A&C). Additionally, the proposed stimulation method performed significantly better than tDCS alone (mean ± SEM, Δ CL tDCS-sync_tDCS = 0.100 ± 0.019, Wilcoxon signed-rank test, P tDCS-sync_tDCS = 0.000, Fig. 3E). These results demonstrate the superior effectiveness of synchronized electrical and mechanical stimulations compared to other methods in enhancing tactile localization ability in post-stroke patients.

Table 2
The mean differences, standard errors of mean differences of CL between each pair of experiments, P-value based on bonferroni correction, and 95% confidence interval for differences. The significant p-values are shown by bold face number. (*: The mean difference is significant at the .05 level)

<table>
<thead>
<tr>
<th>Type of stimulations</th>
<th>Mean Difference</th>
<th>Std. Error</th>
<th>P-value</th>
<th>95% Confidence Interval for Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No-tDCS tDCS-sham</td>
<td>0.017</td>
<td>0.011</td>
<td>0.855</td>
<td>-0.015 – 0.048</td>
</tr>
<tr>
<td>tDCS</td>
<td>-0.008</td>
<td>0.010</td>
<td>1.000</td>
<td>-0.036 – 0.021</td>
</tr>
<tr>
<td>tDCS-sync</td>
<td>-0.108*</td>
<td>0.022</td>
<td>0.000</td>
<td>-0.171 – -0.044</td>
</tr>
<tr>
<td>tDCS-sham No-tDCS</td>
<td>-0.017</td>
<td>0.011</td>
<td>0.855</td>
<td>-0.048 – 0.015</td>
</tr>
<tr>
<td>tDCS</td>
<td>-0.024</td>
<td>0.012</td>
<td>0.306</td>
<td>-0.059 – 0.010</td>
</tr>
<tr>
<td>tDCS-sync</td>
<td>-0.124*</td>
<td>0.022</td>
<td>0.000</td>
<td>-0.190 – -0.059</td>
</tr>
<tr>
<td>tDCS No-tDCS</td>
<td>0.008</td>
<td>0.010</td>
<td>1.000</td>
<td>-0.021 – 0.036</td>
</tr>
<tr>
<td>tDCS-sham</td>
<td>0.024</td>
<td>0.012</td>
<td>0.306</td>
<td>-0.010 – 0.059</td>
</tr>
<tr>
<td>tDCS-sync</td>
<td>-0.100*</td>
<td>0.019</td>
<td>0.000</td>
<td>-0.155 – -0.045</td>
</tr>
<tr>
<td>tDCS-sync No-tDCS</td>
<td>0.108*</td>
<td>0.022</td>
<td>0.000</td>
<td>0.044 – 0.171</td>
</tr>
<tr>
<td>tDCS-sham</td>
<td>0.124*</td>
<td>0.022</td>
<td>0.000</td>
<td>0.059 – 0.190</td>
</tr>
<tr>
<td>tDCS</td>
<td>0.100*</td>
<td>0.019</td>
<td>0.000</td>
<td>0.045 – 0.155</td>
</tr>
</tbody>
</table>

All CL distributions passed the normality test (Kolmogorov–Smirnov test, P No-tDCS = 0.200, P tDCS-sham = 0.200, P tDCS = 0.144, P tDCS-sync = 0.160). To assess the differences in localization abilities among the four experiments, a repeated measure ANOVA model was employed [9]. The results revealed a significant difference among the different stimulation schemes (RMANOVA, F (3, 66) = 22.408, P < 0.001). Further analysis using repeated measures ANOVA with Greenhouse-Geisser correction also showed a statistically significant difference in mean.

4. Discussion
Our findings provide valuable insights into the effectiveness of different stimulation methods in improving tactile localization ability in post-stroke patients. The results indicate that the application of tDCS sham, which does not involve actual electrical stimulation, does not significantly impact the patients' localization ability. However, when a steady DC stimulation is applied, there is a noticeable increase in the patients' ability to localize physical stimulation, although the improvement is not statistically significant compared to the absence of electrical stimulation.

In contrast, the synchronized application of DC stimulation with mechanical stimulation significantly enhances tactile localization ability compared to steady DC stimulation alone. This enhancement is also observed when there is no electrical stimulation involved. These observations are based on the performance of the patients in the four experimental conditions.

It is worth noting that electrical stimulation slightly decreased the correct localization ability of patients, as evident from the comparison between tDCS-sham and No-tDCS experiments. However, this difference is not statistically significant. The slight decrease in performance could be attributed to the discomfort experienced by the patients due to the electrodes placed on their brains.

The marginally significant effect of steady electrical stimulation on tactile localization ($P_{tDCS_tDCS-sham} = 0.035$, Fig. 3E) highlights the potential of tDCS in modulating neural firing probabilities. Our results suggest that the failure in localizing touch stems from insufficient neural activity in the S1 area of the brain triggered by mechanical stimulation alone. In contrast, the electrical pulses generated by tDCS stimulate the brain area, increasing the probability of generating action potentials in response to mechanical stimulation and facilitating successful localization perception. However, due to the adaptation effect in the brain, the impact of steady tDCS on enhancing neural activity in response to mechanical stimulation is less pronounced compared to synchronized tDCS.

Overall, our study demonstrates that synchronized electrical and mechanical stimulation yields superior results in improving tactile localization ability in post-stroke patients. These findings highlight the potential of simultaneous stimulation methods in the treatment and rehabilitation of patients with impaired sensory perception.

### 6. Conclusion

In conclusion, our study introduces a novel treatment approach for enhancing the localization ability of post-stroke patients by synchronizing mechanical stimulation with DC stimulation of the somatosensory region. Building upon our previous findings that demonstrated the effectiveness of synchronizing AC stimulation with physical therapy in improving motor function in stroke patients, [16] we propose that synchronization can serve as a fundamental principle for enhancing various aspects of stroke patients' abilities.

Considering the neuroplasticity-altering effects of tDCS, [24, 25] we anticipate that the long-term treatment of stroke patients using this synchronized stimulation approach will yield promising results.
Exploring the long-term effects and benefits of synchronized stimulation in stroke patients represents a compelling avenue for future research.

Overall, our findings offer valuable insights into the potential of synchronized stimulation as a novel treatment strategy to enhance the localization ability of post-stroke patients. Further investigations into the broader application of synchronization in stroke rehabilitation hold significant promise for improving patient outcomes and quality of life.

**Declarations**

**Competing interests:**

The authors declare that they have no competing interests.

**Ethics approval and consent to participate Consent for publication:**

Ethics approval was obtained for this study, and all participants provided informed consent to participate. Additionally, consent for publication was obtained from the participants, ensuring their anonymity and confidentiality.

**Funding:**

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**Availability of data and materials:**

All datasets and materials utilized in this study are available upon request.

**Authors' contributions:**

All authors contributed to the conception and design of the study. Zahra Bahmani and Mohammad Rostami conducted the data collection and analysis. Maryam Ahmadi drafted the initial manuscript, Mojtaba Barzegar verified the final version of it and all authors critically reviewed and edited the manuscript. All authors have read and approved the final version of the manuscript.

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References


**Figures**

![Figure 1](image-url)
Different types of the applied stimulations. Only mechanical stimulation was applied in the first experiment. In the second experiment, a sham electrical stimulation was applied besides the mechanical stimulation. In the third experiment, a steady electrical stimulation was applied besides the mechanical stimulation. In the last experiment, an electrical stimulation was applied in a synchronized manner with the mechanical stimulation.

**Figure 2**

Statistical measurements of four experiments. The central lines indicate the median, and the bottom and top edges of the boxes show the 25th and 75th percentiles, respectively.
Figure 3

CL is significantly increased by means of synchronized localization. A) Scatter plot of CL values for No-tDCs experiments vs. tDCs-sync experiment. B) Scatter plot of CL values for No-tDCs experiments vs. tDCs experiment. C) Scatter plot of CL values for No-sham experiments vs. tDCs-sync experiment. D) Scatter plot of CL values for tDCS-sham experiments vs. tDCs experiment. E) Scatter plot of CL values for
tDCs experiments vs. tDCs-sync experiment. F) Scatter plot of CL values for No-tDCs experiments vs. tDCs-sham.