# Effect of HD-tDCS and Digital Rehabilitation on Distal Motor Function and Cortical Hemodynamic Responses: A Confirmatory RCT

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## Synopsis

This confirmatory RCT investigates HD-tDCS combined with digital rehabilitation in 58 chronic stroke patients. While the primary outcome (FMA-UE Total) showed no significant group difference ($p$=0.1067), the experimental group exhibited significant improvement in the FMA-UE Wrist sub-score ($p$=0.0129). Concurrent fNIRS analysis revealed a significantly increased hemodynamic response in the ipsilesional sensorimotor area (Channel 59) and strengthened functional connectivity between the primary motor cortex and prefrontal cortex. These findings suggest that the intervention specifically modulates distal motor recovery and facilitates neuroplasticity via hemodynamic regulation.

## Background

Stroke remains a leading cause of long-term disability, with over 40% of survivors suffering from persistent upper limb impairments. High-definition transcranial direct current stimulation (HD-tDCS) offers precise cortical targeting compared to conventional tDCS. Prior studies identified the ipsilesional primary motor cortex (M1) and anterior intraparietal sulcus (aIPS) as key targets for motor recovery[1, 2]. This multicenter, randomized, double-blind, sham-controlled trial aims to confirm the clinical efficacy and safety of HD-tDCS combined with task-based digital rehabilitation. Furthermore, integrated functional near-infrared spectroscopy (fNIRS) was utilized to investigate functional cortical hemodynamics, focusing on task-related responses and connectivity to elucidate neural mechanisms underlying recovery.

## Methods

This multicenter, randomized, parallel-group, double-blind, sham-controlled superiority trial enrolled 58 participants with chronic unilateral stroke (FMA-UE score 25–58) from two clinical sites (Jeonbuk National University Hospital and Myongji Choonhey Rehabilitation Hospital) [3]. Participants were randomized to receive either active HD-tDCS or sham stimulation, both combined with standardized digital upper limb rehabilitation. The intervention consisted of 10 sessions over 4 weeks (40 mins/session). Each session comprised 10 minutes of resting-state

HD-tDCS, followed by 20 minutes of concurrent HD-tDCS and task-based digital rehabilitation, and concluded with 10 minutes of digital rehabilitation alone. Active HD-tDCS was administered using the NT Brain 48CH (CyberMedic Co., Ltd., Republic of Korea), delivering 1.0 mA anodal stimulation targeting the ipsilesional M1 and aIPS. For left hemisphere lesions, anodes were placed at C1 and CP1 with return cathodes at Cz, CPz, FC3, P3, and CP5; this montage was mirrored symmetrically for right hemisphere lesions to modulate motor and sensory integration networks. The sham group received a brief ramp-up/ramp-down protocol to mimic sensory sensations without sustained current. The digital rehabilitation utilized the MotoRehab® system (CyberMedic Co., Ltd., Republic of Korea) which includes specific modules designed for functional movements: Touchscreen tasks; Handle rotation tasks requiring pronation/supination; Air bulb squeeze tasks for grip force modulation; and a Finger-tapping module for fine motor control [4].

Clinical outcomes were assessed at baseline and post-intervention (4 weeks). The primary outcome was the change in Fugl-Meyer Assessment of Upper Extremity (FMA-UE) total score. Secondary outcomes included the 9-Hole Pegboard Test (9HPT), Grip/Pinch strength, Box and Block Test (BBT), Sequential Finger Tapping Test (SFTT), and SF-36. Concurrently, cortical hemodynamic responses were measured using an 80-channel fNIRS system (NT Brain 48CH) integrated with the tDCS electrodes. Participants performed a digital piano tapping task (block design: 30s task, 30s rest) during fNIRS recording. The fNIRS data were processed using a customized pipeline based on Homer2 in MATLAB [5]. Signal processing included converting light intensity to optical density, removing physiological noise using a bandpass filter (0.01–0.1 Hz), and correcting motion artifacts using a wavelet-based algorithm (IQR=1.5). The modified Beer-Lambert law was applied to calculate oxygenated hemoglobin (HbO) concentration changes. Statistical analyses utilized Analysis of Covariance (ANCOVA) for group comparisons, adjusting for baseline scores.

## Results

Of 58 enrolled participants, 56 (Experimental n=28, Control n=28), were included in the Full Analysis Set (FAS). Safety analysis showed no significant difference in adverse events ($p$=0.6115) and no serious adverse events. Both groups showed significant improvements in FMA-UE Total score ($p$<0.0001). The experimental group showed a greater increase (LS Mean change: 6.61±0.86) than the control group (4.60±0.86), but the difference was not statistically significant ($p$=0.1067). However, a significant group difference was observed in the FMA-UE Wrist sub-score ($p$=0.0129). The experimental group demonstrated superior wrist recovery (LS Mean difference: 1.25 [95% CI: 0.28, 2.22]). Additionally, Per-Protocol Set (PPS) analysis indicated significant improvement in the 9-Hole Pegboard Test only within the experimental group ($p$=0.0371).

Functional cortical hemodynamics analysis revealed distinct activation patterns. The experimental group showed broad HbO increases across the ipsilesional motor cortex. Specifically, Channel 59 (CP1-CPz region) showed a statistically significant difference ($p$<0.05) in ANCOVA; the hemodynamic response increased in the experimental group (0.09±0.30) but decreased in controls (-0.06±0.30). Regarding functional connectivity, the experimental group exhibited significantly strengthened connectivity between the ipsilesional M1 and prefrontal cortex (PFC). Interaction analysis confirmed increased inter-hemispheric connectivity (F3–P3, FC3–FC4) in the experimental group compared to controls.

## Discussion

This confirmatory trial demonstrates that concurrent HD-tDCS and digital rehabilitation is safe and benefits distal upper limb recovery. Although the primary endpoint (total FMA-UE) did not reach statistical significance, likely due to the ceiling effect of the intensive digital rehabilitation provided to the control group, the significant improvement in wrist function is clinically meaningful, as distal

movements are often resistant to conventional therapy. The fNIRS results provide a robust hemodynamic basis for these gains. The increased hemodynamic response in the CP1-CPz region aligns with the stimulation targets, validating focal modulation. Furthermore, strengthened M1-PFC connectivity suggests the intervention facilitates motor planning networks to support functional execution. These findings support HD-tDCS as an effective adjunct to digital rehabilitation for enhancing neuroplasticity and distal motor recovery

## Disclosures

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