TMU-Joint Institutional Review Board

Title:

Transcranial Electrical Stimulation with Special Waveform for

Upper Extremity Rehabilitation for Patients with Stroke

Approval Number: N201702070

Date: 2020/01/31

Study Protocol and Statistical Analysis Plan

➢ **Participants**

The present study is a single-blinded, randomized controlled trial pilot study performed at Taipei Medical University Hospital in Taiwan. Experiments is conducted under a protocol approved by the Joint Institutional Review Board of Taipei Medical University with registration number (N201702070). All experiments in this research are performed in accordance with the relevant guidelines and regulations at Taipei Medical University.

Potential participants are identified from Taipei Medical University Hospital. participants (n= 24) are eligible according to the following criteria and consented to take part. The flowchart for the inclusion of patients is as below text. We include patients with ischemic or hemorrhagic chronic stroke diagnosed by the neurologist and meeting the following inclusion criteria: (1)aged ≥20 years; (2) unilateral cerebral stroke with hemiplegia and Brunnstrom stage IV-V;(3) adequate understanding of verbal/written information and physically able to complete the motor learning of functional tasks with the affected hand. Exclusion criteria are as follows: (1) upper motor neuron impairment (2) autonomic nervous system is not stable (3) extremely sensitive to electrical stimulation and cannot tolerate it (4) contractures in the upper extremity or limitation of joint motion (5) severe spasticity (6) myositis ossificans (7) a history of arrhythmia (8) medical electronic device implants, such as a pacemaker (9) decubitus or scalp wounds (10) metal head or neck implants (11) severe cognitive dysfunction or active psychiatric diseases, such as schizophrenia or dissociative identity disorder (12) a history of seizure or organic brain disease (13) severe traumatic brain injury (14) drug or alcohol abuse (15) malignant tumor or autoimmune rheumatic disease, such as systemic lupus erythematosus, rheumatoid arthritis, or ankylosing spondylitis .

➢ **Experimental Protocol and Design**

Participants were randomly assigned to a conventional rehabilitation (CR) combined with real-tDCS+iTBS (experimental group) or sham-CR (control group) using a computer-generated randomized scheme. Randomization, functional outcome measurements, and data analysis were performed by trained research staffs who were not involved in the intervention. All participants received the similarly conventional rehabilitation therapy and duration of real/sham-tDCS+iTBS stimulation in both groups. Conventional rehabilitation treatments (includes fine motor skill training, normal limb posture, active range of motion exercises, muscle strengthening exercises) were conducted by certified occupational therapists who were blinded to the group assignment and trained according to

the investigator's protocol. This experimental protocol consisted of 18 sessions, a 20-min stimulation program per session during the 1 hour conventional rehabilitation program per session activity, 3 days per week for 6 weeks.

➢ Outcome Measures.

A. _Experimental Protocol and Design_

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B. _Fugl-Meyer Assessment-Upper Extremity (FMA-UE)_

At the week before treatment initiation (baseline), clinical and demographic characteristics for each patient were collected. For all groups, the functional outcomes were measured at the baseline, immediately, and 6 weeks after 18 therapeutic sessions (post-treatment) by a researcher blinded to which subjects are receiving the real treatment. The primary outcome of the study was the Fugl-Meyer Assessment-Upper Extremity (FMA-UE). The FMA-UE was performed (score ranges from 0 to 66) to assess upper limb motor recovery. This test has been considered as core measures to detect changes in motor recovery in stroke and rehabilitation trial. [Hsieh, 2009]. The each tasks is rated from 0 to 2, with a higher score representing better hand function performance of stroke patients.

C. _Jebsen-Taylor Hand Function Test (JTT)_

The JTT of hand function is a widely used to assess a broad range of functional hand motor skills that reflects activities of daily living. JTT has shown to be a reliable, valid, and normative data are available at all ages and both genders. We included in our analyses seven subtests of the JTT: writing, turning cards, picking up small objects, picking up beans

with a tea spoon, stacking checkers, lifting light cans and lifting heavy cans. Participants were instructed to perform task as fast and accurately as possible. Total JTT time and subtest JTT times (maximum measure time is 45 sec for each subset) were recorded for analysis.

D. *Finger-to-Nose Test (FNT)*

The FNT is often used to assess upper-limb coordination after stroke. While the patients sat on the chair with the examiner in front of them, they were asked to alternately touch their nose and then extend their finger to touch the examiner's finger as quickly as possible. The numbers of touch events within 1 minute were recorded for analysis.

➢ Statistical Analysis

Normality will be assessed using Kolmogorov–Smirnov tests and most of the outcome measures are not normally distributed. Therefore, nonparametric statistical analyses are used to assess the data. Baseline demographic and clinical measures (mean, standard deviation, and median) are compared between two groups using the Mann–Whitney U-test for continuous variables or Pearson's chi-squared test for categorical variables. The primary and secondary outcome measures are analyzed by Wilcoxon matched-pairs signed-ranks test to investigate time effects (baseline and post-treatment) within groups. Mann-Whitney rank sum test is used to test differences in outcomes among groups. Change in subsets JTT times after stimulation in percentage are calculated according to the following equations: Change in % = (Baseline/Post-treatment *100–100). Statistically significant differences are considered at $p < 0.05$. Statistical analysis is performed using SigmaPlot, version 10.0 (Systat Software, Inc., USA).