Transcranial Direct Current Stimulation for Stroke

Brief Summary: Stroke is the second most common cause of death worldwide, and a major global cause of disability. Approximately 80% of all strokes are ischemic. At present, the only effective and proven treatment for acute ischemic stroke is intravenous thrombolysis with tissue plasminogen activator (t-PA) when given within 4.5 hours after stroke onset. In addition to intravenous thrombolysis, recently thrombectomy has also become a proven effective treatment for acute ischemic stroke within six hours after stroke onset. Although the rate at which intravenous thrombolysis and thrombectomy is given has increased, considering the brief window of time for administration and the risk of bleeding, only a few people with acute ischemic stroke can benefit from these treatments. Newer and safer treatments, especially with longer treatment windows, are urgently needed to benefit more people with acute ischemic stroke. In addition, some other treatments may be given along with intravenous thrombolysis and thrombectomy to help treat the residual problems suffered by people with stroke, such as paralysis, language problems, and visual neglect.

Current rehabilitation approaches have limited effectiveness in improving activities of daily living (ADLs) performance, function, muscle strength and cognitive abilities (including spatial neglect) after stroke, but a possible adjunct to stroke rehabilitation might be non-invasive brain stimulation by transcranial direct current stimulation (tDCS) to modulate cortical excitability, and hence to improve ADL performance, arm and leg function, muscle strength and cognitive abilities (including spatial neglect), dropouts and adverse events in people after stroke.

Detailed Description: The research will be developed in São José Hospital of Santa Casa de Misericórdia de Porto Alegre. After the selection of patients for eligibility criteria they will be randomized into Transcranial Direct Current Stimulation group or sham group. First all patients will be evaluated, and subsequently the patients in the C-tDCS group will be 6 dose tiers, NXXXXXXXXXXXXXXXXXX. There will be 6 dose tiers, reflecting increasing intensity and duration of stimulation: Tier 1 - 1 mA, single 20 - min cycle; Tier 2- 2 mA, single 20 min cycle; Tier 3 - 1 mA, 2 cycles of 20 min/20 min off; Tier 4- 2 mA, 2 cycles of 20 min/20 min off; Tier 5 - 1 mA, 3 cycles of 20 min/20 min off; Tier 6 - 2 mA, 3 cycles of 20 min/20 min off (Treatment open to discussion based on the proteins: Klotho, SDF…).

Other Name: C-tDCS

Conditions: Stroke Acute

Disease Keywords: Stroke; Electrical Stimulation, Transcranial Direct Current Stimulation

Study Design Study Type: Interventional Primary

Purpose: Treatment Study

Phase: 3

Interventional Study Model: Parallel Assignment

Number of Arms: 2

Masking: Single (Outcomes Assessor)

Allocation: Randomized

Enrollment: 10 [Anticipated]

Arms and Interventions

Experimental: Patients will be randomized to active treatment (C-tDCS) vs sham stimulation in a 3:1 ratio. There will be 6 dose tiers, reflecting increasing intensity and duration of stimulation: Tier 1 - 1 mA, single 20 -min cycle; Tier 2- 2 mA, single 20 min cycle; Tier 3 - 1 mA, 2 cycles of 20 min/20 min off; Tier 4- 2 mA, 2 cycles of 20 min/20 min off; Tier 5 - 1 mA, 3 cycles of 20 min/20 min off; Tier 6 - 2 mA, 3 cycles of 20 min/20 min off. (Treatment open to discussion based on the proteins: Klotho, SDF…)

Other Name: C-tDCS

No Intervention: Patients will be randomized to active treatment (C-tDCS) vs sham stimulation in a 3:1 ratio. Patients in the sham stimulation arm at all the tiers will have the cap and electrodes in place, and sham switch moved but without prolonged delivery of electrical stimulation.

Assigned Interventions:

Other Names: (C-tDCS)

Outcome Measures

Primary Outcome Measure: the rate of early neurologic deterioration in the active treatment arm compared to sham arm, and between higher and lower dose tiers.

Early neurological deterioration will be defined as worsening ≥ 4 on NIHSS during the 24-hour period after stimulation without intracranial

hemorrhage. The treatment will be considered to have exhibited adequate safety if tDCS results in lower or equivalent rates of early neurological deterioration compared to sham.

Secondary Outcome Measure:

1. the rate of mortality in the active treatment arm compare to sham arm, and between higher and lower dose tiers. [Time Frame: By day 90 post stimulation

2. the rate of all serious adverse events occurring during the 90 days of study participation in the active treatment arm compare to sham arm, and between higher and lower dose tiers. [Time Frame: By day 90 post-stimulation]

A serious adverse event is any adverse event that is fatal, is life-threatening, is permanently or substantially disabling, requires or prolongs hospitalization, or requires medical or surgical intervention to prevent one of the above outcomes. The rate of serious adverse events will be compared between the active treatment and sham patients, and between higher and lower dose tiers. The treatment will be considered to have exhibited adequate safety if tDCS results in lower or equivalent rates of serious adverse events compared to sham.

3. Exploratory Clinical Efficacy Outcome: examining the clinical outcomes of early neurologic deficit evolution, and 3-month global disability and health-related quality of life. [Time Frame: At day 90 post stimulation]

Four clinical outcome measures will be assessed at 90 days: the modified Rankin Scale (mRS), a rating of global disability; the Barthel Index (BI), a

measure of instrumental activities of daily living; the National Institutes of Health Stroke Scale (NIHSS), a measure of neurologic deficit severity; and the EuroQol (EQ-5D), an assessment of health-related quality of life; and AMC Linear Disability Scale, a granular degree of disability.

Clinical efficacy endpoints will be characterized in the active and sham patients, and in higher and lower dose tiers. The study is underpowered to definitely assess efficacy; however, the treatment may be considered to be efficacious if tDCS results in an improved clinical outcome compared to sham.

Eligibility: Minimum Age: 18 Years and older (Adult, Older Adult)

Maximum Age: 60 Years

Sex: All

Inclusion Criteria:

1. New focal neurologic deficit consistent with AIS
2. NIHSS≥4 or NIHSS <4 in the presence of disabling deficits
3. Age>18;
4. Presence of any cortical vessel occlusion including ICA, branches of MCA, Anterior Cerebral artery (ACA), Posterior Cerebral artery (PCA), Posterior-Inferior cerebellar artery (PICA);
5. Presence of salvageable penumbra with Tmax> 6 sec/ ischemic core volume (ADC < 620 μm2/s or rCBF< 30%) ≥ 1.2
6. Patient ineligible for IV tPA, per national AHA/ASA Guidelines
7. Patient ineligible for endovascular therapy per AHA/ASA national Guidelines - one or more of: poor prestroke functional status (mRS score >1), mild neurological symptoms (NIHSS <6), large ischemic core (ASPECTS <6), thrombectomy not technically performable due

to severe vessel tortuosity, cervical artery chronic occlusion, or other unfavorable angioarchitectural features that preclude endovascular access to the target intracranial vessel. 8) Subject is able to be treated with tDCS within 24 hours of last known well time;

Exclusion Criteria:

1. Acute intracranial hemorrhage
2. Evidence of a large Ischemic core volume (ADC < 620 µm2/s or rCBF< 30%) ≥ 100
3. Presence of tDCS contraindications - electrically or magnetically activated intracranial metal and non-metal implants.
4. Severe MR contrast allergy or renal dysfunction with eGFR<30ml/min, precluding MRI gadolinium or CT iodine contrast
5. Pregnancy
6. Signs or symptoms of acute myocardial infarction, including EKG findings, on admission
7. Suspicion of aortic dissection on admission
8. History of seizure disorder or new seizures with presentation of current stroke
9. Evidence of any other major life-threatening or serious medical condition that would prevent completion of the study protocol including attendance at the 3-month follow-up visit
10. Concomitant experimental therapy
11. Preexisting scalp lesion at the site of the stimulation or presence of skull defects (may alter current flow pattern)

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