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Transcranial Direct Current Stimulation for Post-stroke Motor Recovery: A Phase II StrokeNet Trial (TRANSPORT2)

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Background

- 795,000 strokes occur each year in the US, globally, over 15 million.
  - In the US, Stroke is the 5th leading cause of death,
  - the #1 cause of long-term disability, and
  - motor deficit is the most common complication.
- Potential for post-stroke motor recovery depends on the degree of injury to descending motor pathways.
- Multiple forms of neuroplasticity (e.g., unmasking, axonal sprouting, cortical reorganization, modulation of abnormal interhemispheric interactions) can also contribute to recovery.

Hypotheses:

1. When combined with rehabilitation therapy, tDCS can further facilitate motor skill acquisition via increased input to the cortex, and
2. Using 2 or 4 mA current combined with Modified Constraint-Induced Motor Therapy (mCIMT), an effective, standardized peripheral therapy designed to overcome learned non-use phenomenon in stroke patients, will lead to greater sustained motor improvement than either mCIMT or tDCS alone.

Aims

Primary aim: To determine whether there is an overall treatment effect among the three dosing groups (sham, 2mA and 4mA) immediately after the 2-week intervention. Sustained effects will be assessed at 1 and 3 months post-intervention.

Secondary aims: To assess safety, tolerability, and feasibility in a multisite Phase II StrokeNet trial.

Exploratory aim: To examine whether structural (weighted corticospinal tract lesion load (wCST-LL)), or functional (Motor Evoked Potentials (MEPs)) integrity of the descending motor tract (or both) correlate with changes in FM-UE scale, and evaluate the utility of these measures as biomarkers for patient selection in a Phase III study.

Methods

Recruitment & Screening:

- Subjects will be identified at inpatient hospital & rehab settings, as well as via stroke databases and self-selection,
- Screened for eligibility through medical records,
- Contacted to discuss study details/determine interest.
- Phone screening will be done for patients/families who initiate contact and wish to participate.

Imaging Measures:

- Pre-Tx MRI to determine structural integrity of the descending motor tract (wCST-LL),
- Pre- and post-Tx DTI to measure any change in FA values that correlate with treatment-induced behavioral changes
- TMS to determine presence and measure size of MEPs

Interventions:

- Modified Constraint-induced Motor Therapy (mCIMT) 90-120min/day for 10 days + home practice.
- tDCS (2 mA, 4 mA, or Sham) for the first 30 minutes of each treatment session.

Outcome Measures

- Primary outcomes:
  - Fugl-Meyer Upper-Extremity Scale (FM-UE; Motor Impairment)
  - Stroke Impact Scale-Hand Subscale (SIS; Quality of Life)
- Secondary outcomes:
  - Wolf Motor Function Test Time (WMFT; Functional Motor Activity)
  - Stroke Impact Scale-Hand Subscale (SIS; Quality of Life)

Participants: 129 patients (43/Tx Group; enrolled at 12 sites; 3.5 yrs)

Inclusion Criteria:

- 18-80 years old (any gender)
- 1-5 months post-onset of 1st-ever ischemic stroke
- >10° active wrist extension, thumb abduction/extension+ 2 digits
- Unilateral limb weakness; FM-UE score ≤ 54 (max=66)
- Absolute difference of ≤ 2 in FM-UE scores between Baseline Ax’s
- Pre-stroke mRs ≤ 2

Exclusion Criteria:

- Primary hemorrhagic, bihemispheric, or bilateral brainstem stroke
- Medication/Tx that would interfere with tDCS or mCIMT
- Other co-existent neuromuscular disorders affecting UE
- Moderate to severe cognitive impairment (MOCA score < 18/30)
- Medically uncontrolled depression/neru-psych disorders
- Uncontrolled hypertension
- Contraindications for MRI/tDCS/TMS
- Inability to remain in the study for 6 months
- Concurrent enrollment in another study

References


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