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The effect of transcranial direct current stimulation on motor sequence learning and upper limb function after stroke

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HIGHLIGHTS

- Stroke survivors demonstrated sequence specific learning, irrespective of transcranial direct current stimulation (tDCS) condition.
- Improvement in the Jebsen Taylor test was seen after unilateral motor cortex tDCS but not after bihemispheric motor cortex tDCS.
- Changes in performance with tDCS were independent of changes in transcallosal inhibition.

ABSTRACT

Objective: To assess the impact of electrode arrangement on the efficacy of tDCS in stroke survivors and determine whether changes in transcallosal inhibition (TCI) underlie improvements.
Methods: 24 stroke survivors (3–124 months post-stroke) with upper limb impairment participated. They received blinded tDCS during a motor sequence learning task, requiring the paretic arm to direct a cursor to illuminating targets on a monitor. Four tDCS conditions were studied (crossover); anodal to ipsilesional M1, cathodal to contralesional M1, bihemispheric, sham. The Jebsen Taylor hand function test (JTT) was assessed pre- and post-stimulation and TCI assessed as the ipsilateral silent period (iSP) duration using transcranial magnetic stimulation.
Results: The time to react to target illumination reduced with learning of the movement sequence, irrespective of tDCS condition ($p > 0.1$). JTT performance improved after unilateral tDCS (anodal or cathodal) compared with sham ($p < 0.05$), but not after bihemispheric ($p > 0.1$). There was no effect of tDCS on change in iSP duration ($p > 0.1$).
Conclusions: Unilateral tDCS is effective for improving JTT performance, but not motor sequence learning.
Significance: This has implications for the design of future clinical trials.

1. Introduction

Stroke is a leading cause of adult disability and many people are left with impairments and are dependent on others for activities of daily living (Dobkin, 2005; DOH, 2007; Veerbeek et al., 2011). Strategies to improve plasticity and enhance motor learning are needed. One potential approach is to use transcranial direct current stimulation (tDCS) to enhance the effect of physical therapy.

After unilateral stroke it has been proposed that there is an interhemispheric imbalance in transcallosal inhibition between the two motor cortices with excess inhibition of the ipsilesional primary motor cortex (M1) by the "undamanged" contralesional M1 (Murase et al., 2004; Nowak et al., 2009; Takeuchi et al., 2010; Takeuchi and Izumi, 2012; Wessel et al., 2015). The result is that the ipsilesional M1 is "doubly disabled" both by the lesion and by the excess inhibition from the contralesional hemisphere.

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To tackle this imbalance three main strategies for delivering tDCS have been proposed; (i) anodal to increase excitability of the ipsilesional M1, (ii) cathodal to decrease excitability of the contralesional M1 or (iii) both anodal and cathodal applied simultaneously (bihemispheric). Bihemispheric stimulation could hypothetically provide additional benefit over unilateral by targeting both cortices concurrently. However, the impact of electrode arrangement on motor learning and function after stroke is unclear and requires systematic investigation.

Physical therapy can be regarded as a form of motor learning in which the damaged motor system is re-trained to optimise the function of its remaining output. Experimentally, motor learning is commonly assessed as changes in motor preparation, speed and accuracy with the repetition of a movement sequence or pattern. However, there are very few paradigms which enable assessment of motor sequence learning using the paretic arm in stroke survivors with upper limb impairment. We developed such a paradigm, requiring gross movements of the arm to direct a cursor to targets on a monitor which illuminated in a repeating order. Here we used this paradigm to systematically assess the impact of tDCS electrode arrangement on within session motor sequence learning and upper limb function in stroke survivors with mild and moderate impairment. We used the Jebsen Taylor hand function test (JTT) (Jebsen et al., 1969) as a marker of upper limb function as this timed test is valid and responsive (Jebsen et al., 1969; Beebe and Lang, 2009) and has been used previously to detect changes within an experimental session (Fregni et al., 2005; Hummel et al., 2005; Mahmoudi et al., 2011). We also aimed to determine whether changes in learning or JTT performance with tDCS would depend on changes in transcallosal inhibition (TCI). We hypothesised that within-session improvements in learning and JTT performance would be evident with active tDCS in comparison with sham. Based on the interhemispheric imbalance model we predicted that bihemispheric tDCS would provide additional enhancement over unilateral stimulation and that improvements would be associated with an increase in TCI from the ipsilesional to the contralesional M1.

2. Methods

2.1. Participants

Potential participants were identified between March 2014 and May 2016 from three National Health Service (NHS) trusts, stroke user groups and word of mouth. Eighty stroke survivors underwent an initial screening and agreed to be followed up. Of these, 25 participants were eligible and consented to take part (Fig. 1). Participant characteristics are presented in Table 1. Time since stroke and stroke location were determined from medical records.

Inclusion criteria were; aged >18 years, first monohemispheric stroke >3 months duration, unilateral upper limb impairment and physically able to complete the motor sequence learning task with the affected hand. Exclusion criteria were; contraindications to transcranial magnetic stimulation (TMS) such as epilepsy or seizures, cardiac pacemakers or metal implants in the head. All participants provided written informed consent and the study was approved by the National Research Ethics Service and adopted by the UK National Institute for Health Research (NIHR) clinical research portfolio (UKCRN ID: 16299).

2.2. Study design

This was a single-blinded crossover study. Participants attended five sessions in total with the time of day kept as consistent as possible and each session lasting ~1.5 h. The first session was for familiarisation with the protocols. The remaining four were experimental sessions; tDCS was delivered during the motor sequence learning task, and the JTT and TCI were assessed pre- and post-stimulation.

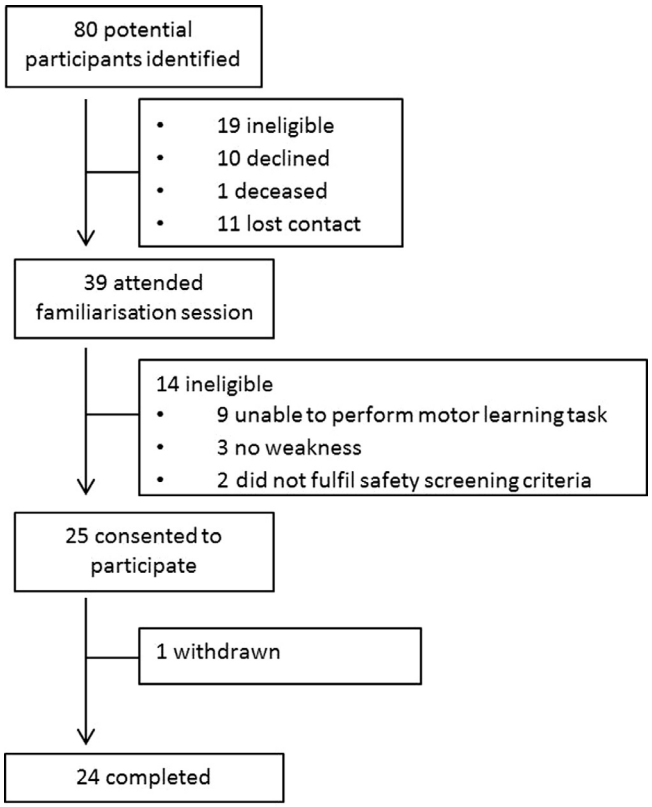

Fig. 1. Recruitment of participants.

2.2.1. Familiarisation session

Participants practiced the motor sequence learning task and the JTT in order to minimise potential differences between sessions due to familiarisation with the protocols. Familiarisation of the JTT involved 10 repetitions of each task, or until performance time stabilised (mean (SD): 7 (2) repetitions). For the motor sequence learning task, participants completed as many repetitions as necessary to ensure they felt comfortable with the use of the computer mouse with the affected hand and understood the purpose of the task (mean (SD): 11 (6) repetitions).

2.2.2. Experimental sessions

The four experimental sessions were conducted using a within-subject crossover design with sessions at least one week apart (mean (SD): 11 (7) days). The crossover design was chosen in an attempt to control for inter-individual variation in upper limb function and ability to learn the movement sequence. In each session, participants initially performed three repetitions of the JTT, followed by TMS (to localise M1 and assess TCI). The tDCS was then delivered for the first 20 min of the motor sequence learning task (which took on average 24 min to complete). TCI was then re-assessed and an additional three repetitions of the JTT performed. One participant was unable to tolerate long durations of TMS and so it was used to localise M1 but TCI was not assessed. Two other participants did not undergo TMS (one found it painful, one had a seizure >30 years earlier) and M1 was localised using C3/C4 of the 10–20 EEG system. Similarly, this method was used to locate the ipsilesional M1 if it was not possible to elicit a motor evoked potential (MEP).