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Transcranial Direct Current Stimulation to Optimise Participation in Stroke Rehabilitation – A Sham-Controlled Cross-Over Feasibility Study

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ABSTRACT

BACKGROUND: Fatigue and attentional decline limit the duration of many therapy sessions in older adults poststroke. Transcranial direct current stimulation (tDCS) may facilitate participation in rehabilitation, potentially via reduced fatigue and improved sustained attention poststroke.

OBJECTIVE: To evaluate whether tDCS results in an increase in the number of completed rehabilitation therapy sessions in stroke survivors.

METHODS: Nineteen participants were randomly allocated to receive 10 sessions of 2-mA anodal (excitatory) tDCS, or sham tDCS, applied to the left dorsolateral prefrontal cortex (DLPFC) for 20 minutes within 1 hour prior to the first rehabilitation therapy session of the day. After a 2-day washout period, participants then crossed-over. Researchers applying the tDCS, and those recording measures were blinded to group allocation. The number of first rehabilitation therapy sessions completed as planned, as well as the total duration of rehabilitation therapy, were used to determine the influence of tDCS on participation in stroke rehabilitation.

RESULTS: The total number of first therapy sessions completed as planned did not vary according to group allocation (111 of 139 sessions for tDCS, 110 of 147 sessions for sham treatment; chi-square 1.0; \( P = .31 \)).

CONCLUSIONS: Our results suggest that, while tDCS to the DLPFC was well tolerated, it did not significantly influence the number of completed rehabilitation therapy sessions in stroke survivors.

KEYWORDS: Stroke rehabilitation, transcranial direct current stimulation, fatigue, attention, noninvasive brain stimulation

Introduction

Attention deficits may affect the ability of older adults to engage in rehabilitation poststroke.1 In addition, fatigue is very common poststroke. Fatigue is a complex impairment. Reduced cortical excitability is postulated to be one factor contributing to poststroke fatigue.2 Thus, fatigue and attentional decline may limit rehabilitation therapy session duration in older adults poststroke.1,2 Because rehabilitation is typically offered only in the initial months poststroke, it is critical that stroke survivors engage in as much therapy as possible during this time. The mean physiotherapy session treatment duration in a large published series was 38 ± 17 minutes.3 We identified that many patients, particularly those with severe stroke, are not able to stay alert for the duration of their therapy sessions and often cannot complete their therapy due to fatigue, attentional decline, or loss of concentration. In local audit data, the mean session duration of therapy sessions among 14 stroke survivors in the Bentley Hospital Stroke Rehabilitation Unit (SRU) was 34 ± 23 minutes. These published international data, and our local data, are both far below the recommended durations of rehabilitation therapy (at least 3 hours a day of scheduled therapy)4 suggesting the importance of investigating interventions that can improve duration and the number of therapy sessions.

There is preliminary evidence that noninvasive brain stimulation (NIBS) can enhance alertness and attention poststroke.5,6 Compared with other NIBS techniques such as repetitive transcranial magnetic stimulation, transcranial direct current stimulation (tDCS) offers a reliable safety profile,7 affordability, ease of application, and sophisticated sham mode which allows for blinded control in clinical trial settings.8 Transcranial direct current stimulation is one of the most commonly used adjuvant NIBS techniques and has been shown to augment the recovery of upper limb movement and function.
Transcranial direct current stimulation acts to modulate cortical excitability by application of weak electrical currents (up to 2 mA) via electrodes applied to the scalp. Depending on the current polarity, neuronal firing rates increase or decrease due to changes in resting membrane potentials, with anodal tDCS increasing the likelihood of neuronal firing and cathodal tDCS decreasing the likelihood of neuronal firing. It has been shown to be safe even when applied acutely (within two days) to the stroke-affected cortex. Previous research has shown stroke survivors demonstrated greater accuracy, but not speed, on a test of executive attention following one session of tDCS compared with sham stimulation. Transcranial direct current stimulation was delivered by a constant current electric stimulator via a pair of rubber surface electrodes overlying a saline infused pad. The anode was applied to the left DLPFC (according to the International EEG 10/20 System), and the cathode was applied to the contralateral supraorbital area. Anodal stimulation consisted of a 30-second current ramp up followed by 19 minutes of constant current stimulation (2 mA) and a 30-second ramp down to zero current (20-minute total protocol); sham stimulation consisted of a 30-second current ramp up (2 mA) followed immediately by a 30-second ramp down to zero current. Researchers applying the tDCS and those recording measures were blinded to group allocation. Outcome measures were (a) whether the first rehabilitation therapy session of the day immediately following application of tDCS was completed as planned and (b) the cumulative duration (in minutes) of rehabilitation sessions.

Materials and Methods
The study was approved by the Royal Perth Hospital Human Ethics Committee (2016-027) and prospectively registered (ACTRN12616000254493). An investigator provided all participants with a written information sheet, a simplified written summary of the information sheet designed for people experiencing communication impairments, and verbal information about the study. All participants provided written informed consent.

Older adults (60+ years) admitted to the Bentley Hospital SRU with a diagnosis of ischaemic stroke, who clinical staff judged were likely to be inpatients ≥1 month, were eligible to participate. Exclusion criteria included prestroke history of fatigue-related syndromes, unstable comorbid medical or psychiatric disease, history of seizures or metallic foreign body implant, and use of NMDA receptor antagonists or calcium channel blockers (which limit the beneficial effect of tDCS). Participants were randomly allocated to receive 10 sessions (ie, each weekday for 2 weeks) of 2-mA anodal (excitatory) tDCS or sham tDCS, applied to the left DLPFC for 20 minutes. After a 2-day washout period, participants then crossed-over to the other study condition.

Transcranial direct current stimulation was applied within 1 hour prior to the first daily therapy session. Transcranial direct current stimulation was applied in accordance with published guidelines for the safe use of tDCS. Transcranial direct current stimulation was delivered by a constant current electric stimulator via a pair of rubber surface electrodes overlying a saline infused pad. The anode was applied to the left DLPFC (according to the International EEG 10/20 System), and the cathode was applied to the contralateral supraorbital area. Anodal stimulation consisted of a 30-second current ramp up followed by 19 minutes of constant current stimulation (2 mA) and a 30-second ramp down to zero current (20-minute total protocol); sham stimulation consisted of a 30-second current ramp up (2 mA) followed immediately by a 30-second ramp down to zero current. Researchers applying the tDCS and those recording measures were blinded to group allocation. Outcome measures were (a) whether the first rehabilitation therapy session of the day immediately following application of tDCS was completed as planned and (b) the cumulative duration (in minutes) of rehabilitation sessions.

Results
One hundred seventy consecutive patients were screened. The reasons for screen failure were length of stay anticipated to be ≥1 month (n = 64), diagnosis not ischaemic stroke (n = 48), treatment with calcium channel blockers (n = 16), which interfere with tDCS effects, and other (n = 13). Ten patients declined participation. The 19 remaining participants (13 female; 6 male; median age 79 [70.5, 82.5] years) were recruited. The total number of planned first therapy sessions completed did not vary according to group allocation (111 of 139 therapy sessions completed as planned following tDCS of 110 of 147 therapy sessions completed as planned in the sham condition; chi-square 1.0; \( P = .31 \)). Similarly, the proportion of patients completing all first therapy sessions of the day was not different according to group allocation (4 of 16 participants receiving tDCS; 8 of 18 participants receiving sham;
studies have used up to 30 sessions, and that there are some sessions, which we judged would be feasible in a cross-over rhage. It could also be the case that the dose of treatment (10 ever, none of the included patients had a diagnosis of haemor- of patients with a specific aetiology of ischaemic stroke; how- ever, none of the included patients had a diagnosis of haemorrhage. It could also be the case that the dose of treatment (10 sessions, which we judged would be feasible in a cross-over design) in our study was insufficient, given that some previous studies have used up to 30 sessions, and that there are some data10 supporting a dose-response relationship. Similarly, we chose a 2-day washout, which may have been insufficient. Future studies may consider use of a higher numbers of ses- sions over a longer time period or tDCS applied simultaneously with rehabilitation intervention. Finally, we used a clinical endpoint (duration of rehabilitation sessions) as the primary outcome. More sensitive measures of sustained attention, fatigue, and other factors limiting participation in ther- apy, including self-report measures, may be required to demonstrate benefits in subgroups of stroke survivors with fatigue/attention deficits.

The strengths of our study are that participants and assess- sors were blinded to group allocation, and the inclusion of a sham condition, so that participants acted as their own control. The major limitation of our study is the potential for random error, and limited generalisability, because of the small number of participants. These limitations are unfortunately common in many of the studies in this field. There were also methodologi- cal limitations; eg, we did not confirm successful blinding. Further studies with carefully selected subgroups of stroke sur- vivors should be considered. Measurement of fatigue and attention at multiple time points in each 24-hour period would have been desirable, but was not possible in this feasibility study. This study shows that tDCS is feasible for in-patients, and future work should directly measure fatigue and attention to understand whether tDCS can increase engagement in ther- apy via reduction in fatigue and increase in attention.

In conclusion, to our knowledge, this is the first study to explore the use of tDCS to specifically improve attention and reduce the effect of fatigue on treatment tolerance in older stroke survivors. Our results suggest that, while tDCS to the DLPFC was feasible to apply during subacute stroke rehabilita- tion, and was well tolerated, it did not significantly influence fatigue or alertness which are major contributors to a patient’s engagement in therapy. Larger studies are needed to make definitive conclusions about any potential benefit of tDCS to the DLPFC on alertness poststroke in older stroke survivors.

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Author Contributions
All authors contributed to study design and acquisition of data. CEB analysed the data and drafted the manuscript, with critical revision by all authors.

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