



The effects of anodal-tDCS on cross-limb transfer in older adults



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HIGHLIGHTS

- Older adults can develop use-dependent plasticity following motor learning.
- The iM1 modulates cross-limb transfer and is facilitated by tDCS in older adults.
- SIC1 mediates cross-limb transfer but is not influenced by anodal-tDCS.

ABSTRACT

Objective: Age-related neurodegeneration may interfere with the ability to respond to cross-limb transfer, whereby bilateral performance improvements accompany unilateral practice. We investigated whether transcranial direct current stimulation (tDCS) would facilitate this phenomena in older adults.

Methods: 12 young and 12 older adults underwent unilateral visuomotor tracking (VT), with anodal or sham-tDCS over the ipsilateral motor cortex. Transcranial magnetic stimulation (TMS) assessed motor evoked potentials (MEPs) and short interval intracortical inhibition (SICI). Performance was quantified through a VT error. Variables were assessed bilaterally at baseline and post-intervention.

Results: The trained limb improved performance, facilitated MEPs and released SICI in both age groups. In the untrained limb, VT improved in young for both sham and anodal-tDCS conditions, but only following anodal-tDCS for the older adults. MEPs increased in all conditions, except the older adult's receiving sham. SICI was released in both tDCS conditions for young and old.

Conclusion: Following a VT task, older adults still display use-dependent plasticity. Although no significant age-related differences between the outcome measures, older adults exhibited significant cross-limb transfer of performance following anodal-tDCS, which was otherwise absent following motor practice alone.

Significance: These findings provide clinical implications for conditions restricting the use of one limb, such as stroke.

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1. Introduction

The process of healthy ageing leads to progressive degeneration of neural networks that control everyday movements (Ward and Frackowiak, 2003). Several studies show that reduced motor control accompanies ageing, specifically during tasks requiring fine motor control, including external and visual paced movements such as computer tasks (Houx et al., 1993; Smith et al., 1999). Such deficits can lead to a progressive loss in the ability to carry out

everyday tasks, leading to reduced functional independence and quality of life.

Recently, transcranial direct current stimulation (tDCS) has emerged as a promising, non-invasive technique to improve motor performance in older adults and the elderly (Hummel et al., 2010; Zimerman et al., 2012; Goodwill et al., 2013). The application of tDCS over the primary motor cortex (M1) induces transient, polarity specific changes in the neuronal resting membrane potential (Nitsche et al., 2008), with increases in excitability and performance improvements lasting up to 90 min following the cessation of stimulation (Nitsche and Paulus, 2000; Nitsche and Paulus, 2001; Nitsche et al., 2005). Pharmaceutical evidence suggests that the lasting effects of tDCS appear to exhibit mechanisms associated with long term potentiation (LTP), representing an element of

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cortical plasticity (Liebetanz et al., 2002; Nitsche et al., 2003). Given that these processes are also known to be involved in motor learning (Asanuma and Keller, 1991), tDCS may represent a beneficial tool to induce use-dependent plasticity and improve motor performance in older adults.

Following repeated motor practice of a given task (e.g., ballistic contractions), there is mixed evidence as to whether older adults preserve the capacity to form use-dependent plasticity and functional performance improvements. A number of previous studies in older adults have observed a lack of an improvement in functional performance and changes in corticospinal excitability and inhibition, suggesting that there is an age-related decline in the ability to form use-dependent plasticity (Sawaki et al., 2003; Fujiyama et al., 2009; Rogasch et al., 2009). However, more recent literature has suggested that functional improvements following a motor task are similar to their younger counterparts (Cirillo et al., 2011, 2010). Considering these proposed age-related deficits, recent studies have applied tDCS concurrently with motor practice, demonstrating the induction of use-dependent plasticity with subsequent improvements in performance and skill acquisition (Zimerman et al., 2012; Goodwill et al., 2013). Although only preliminary, this data highlights the potential to use tDCS to facilitate the formation of use-dependent cortical plasticity in older adults.

Cross-limb transfer of performance is a well-known phenomenon whereby bilateral performance improvements are attained following unilateral practice, and these improvements appear reflective of use-dependent plasticity within the central nervous system (CNS). Although the mechanisms remain unclear, increased activation of the ipsilateral M1, attributed partially to a release of interhemispheric and/or intracortical inhibition, has recently been suggested as a primary mediator (Perez and Cohen, 2008; Hinder et al., 2010a,b). Cross-limb transfer has been demonstrated following strength, ballistic and motor skill practice such as visuomotor tracking (Imamizu and Shimojo, 1995; Nagel and Rice, 2001; Sainburg and Wang, 2002; Schulze et al., 2002; Perez et al., 2007; Carroll et al., 2008; Lee et al., 2010). However, most previous studies demonstrating performance transfer with unilateral training have been conducted in healthy young adults, and recent evidence has emerged to suggest that older adults exhibit a reduced capacity for cross-limb transfer (Hinder et al., 2010a).

It is widely reported that during unilateral movements, older adults exhibit greater motor overflow to the contralateral limb, often measured through an increase in electromyography (EMG) activity (Bodwell et al., 2003; Hinder et al., 2010a). Although this may be reflective of activation within the ipsilateral M1, a recent study reported that the age-related increase in motor overflow had no preferential effect on the cross-transfer of performance (Hinder et al., 2010a). Therefore, it is likely that the mechanisms mediating cross-transfer may be of a cortical origin (i.e. facilitation or inhibition) and may differ to those involved in motor overflow. Indeed, there is evidence that there is a reduced ability to modulate interhemispheric and intracortical inhibition during different motor tasks in older adults (Sale and Semmler, 2005; Hinder et al., 2010a). Considering that these mechanisms, in particular within the ipsilateral M1, have been proposed to play a role in mediating cross-limb transfer (Hinder et al., 2010b; Hortobágyi et al., 2011; Goodwill et al., 2012), it is possible that the age-related degeneration within these circuits may be contributing to the absence of cross-transfer that has previously been observed in older adults.

Recent data has demonstrated that the addition of tDCS may modulate intracortical inhibition in older adults (Goodwill et al., 2013). Therefore, the use of tDCS may be an effective tool to modulate the release of intracortical inhibition within the ipsilateral M1 and mediate the cross-transfer of performance, but this has not been quantified. Therefore, the aim of this study was to

investigate the efficacy of anodal-tDCS over the ipsilateral M1 in combination with unilateral practice, to enhance performance of the untrained limb in older adults. It was hypothesised that the addition of anodal-tDCS would up-regulate indices of use-dependent plasticity in the ipsilateral M1 and facilitate cross-limb transfer in older adults.

2. Method

2.1. Participants

Twelve healthy older (mean \pm SD; 66.0 ± 1.0 years; male, $n = 6$; female, $n = 6$) and twelve healthy young adults (26.0 ± 1.4 years; male $n = 6$; female $n = 6$) were recruited to participate in this study. All participants were recruited from within the local community in Melbourne, Australia. Participants were excluded from the study if they reported a history of neurological impairment or musculoskeletal injury of the upper limb in the last 12 months or were taking medication known to influence the CNS. One participant reported mild arthritis, however this was not in the wrist. All participants were tested for handedness according to the 10 item version of the Edinburgh Handedness Inventory (mean laterality quotient, 93.0 ± 3.2). Two participants were left handed [mean laterality quotient (-75.0 ± 5.0)] and were not excluded from the analyses, rather, their dominant limb was trained. All participants completed an Adult Safety Screening Questionnaire to determine their suitability for TMS and tDCS application (Keel et al., 2001). Participants were free of any cognitive impairment as assessed by the Mini-Mental State Examination [MMSE; young 29.0 ± 0.3 ; old 29.0 ± 0.5]. All participants completed the long version of the International Physical Activity 33 Questionnaire (IPAQ), consisting of 31 items relating to levels of physical activity, 34 specifically, aerobic exercise (i.e. walking, lifting, running, cycling and swimming) in a range of areas such as leisure, work, active transport, and household activities (group average MET-mins/week = 3370) (Fogelholm et al., 2006). No participants reported playing a long term musical instrument. All participants provided written informed consent prior to participation in the study, which was approved by the Deakin University Human Research Ethics Committee. All procedures were conducted according to the standards established by the Declaration of Helsinki.

2.2. Experimental design

Experimental procedures were identical for both conditions and both age groups and are outlined in Fig. 1. One week prior to baseline assessments participants received familiarisation practice trials with the motor task. All participants were exposed to two experimental sessions involving motor practice of their dominant limb, with either anodal or sham tDCS projecting to the M1 ipsilateral to the training limb. The experiment was a randomised, double-blinded cross-over trial. The order of conditions counter-balanced across participants and separated by a one week wash out period which has been recommended to eliminate carry-over tDCS effects (Nitsche and Paulus, 2001; Nitsche et al., 2008). Participants were examined for baseline measures of corticospinal excitability and intracortical inhibition for both motor cortices, with the order of limb testing randomised across participants. Following baseline testing, participants were asked to perform 15, 10-s bouts of visuomotor tracking of their dominant limb (wrist extensors and flexors). Following motor practice, measurements of motor performance, corticospinal excitability and intracortical inhibition were obtained for both limbs, following the same protocols as the baseline measures. A rest period of five minutes was taken following the training block, to eliminate the potential

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