Ageing Research Reviews 25 (2016) 42–54

Contents lists available at ScienceDirect

Ageing Research Reviews

journal homepage: www.elsevier.com/locate/arr

Review

Does transcranial direct current stimulation enhance cognitive and motor functions in the ageing brain? A systematic review and meta-analysis

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ARTICLE INFO

Article history:
Received 10 June 2015
Received in revised form 9 November 2015
Accepted 16 November 2015
Available online 30 November 2015

Keywords:
Meta-analysis
Transcranial direct current stimulation (tDCS)
Anodal tDCS
Cognitive function
Motor function
Ageing

ABSTRACT

The use of transcranial direct current stimulation (tDCS) to enhance cognitive and motor functions has enjoyed a massive increase in popularity. Modifying neuroplasticity via non-invasive cortical stimulation has enormous potential to slow or even reverse declines in functions associated with ageing. The current meta-analysis evaluated the effects of tDCS on cognitive and motor performance in healthy older adults. Of the 81 studies identified, 25 qualified for inclusion. A random effects model meta-analysis revealed a significant overall standardized mean difference equal to 0.53 (SE = 0.09; medium heterogeneity: $I^2 = 57.08\%$; and high fail-safe: $N = 448$). Five analyses on moderator variables indicated significant tDCS beneficial effects: (a) on both cognitive and motor task performances, (b) across a wide-range of cognitive tasks, (c) on specific brain areas, (d) stimulation offline (before) or online (during) the cognitive and motor tasks. Although the meta-analysis revealed robust support for enhancing both cognitive and motor performance, we outline a number of caveats on the use of tDCS.

Contents

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http://dx.doi.org/10.1016/j.arr.2015.11.004
1568-1637/

1. Introduction

Population ageing is a global phenomenon with the total number of people aged 60 or older worldwide predicted to more than double from 841 million in 2013 to over 2 billion in 2050 (21.1% of the world population). Importantly, the number of people aged 80 years or more within the older population is expected to grow in the same time period from 14% to 19% (392 million persons) and the number of people with dementia is forecast to increase from 44.4 million to 135.5 million (Alzheimers Disease International, 2013; United Nations Department of Economic and Social Affairs, Population Division, 2013).

Normal ageing is associated with progressive decline in cognitive and motor functions especially in basic information processing components, such as processing speed, working memory, and episodic memory. At the neurophysiological level, there is progressive shrinkage with age of grey matter volume in several brain regions and white matter loss, particularly in the prefrontal cortex. Even modest declines in cognitive and motor function can negatively impact on quality of life and the ability to live independently in older adults. Furthermore, signs of cognitive decline, particularly memory loss, are of considerable concern to older individuals because of the possible progression to Alzheimer's disease. Neurologists estimate that delaying onset of Alzheimer's disease by 5 years would reduce the overall prevalence rate by 50%, significantly reducing caregiver burden, institutional care, and enhancing quality of life (Brookmeyer et al., 1998).

Not surprisingly, there has been much recent research interest in discovering non-pharmacological ways in which cognitive and motor decline associated with ageing can be slowed or even reversed. Importantly, neuroscientists agree that the brain, rather than being static after childhood, is constantly adapting to changing conditions throughout adulthood and during physiological ageing. This process, known as neuroplasticity, is the basis for (a) cognitive/motor functions, (b) cognitive/motor learning, and (c) the brain's responses to disease and injury (Berlucchi, 2011). Impaired neuroplasticity mechanisms are frequently linked to cognitive and motor deficits accompanying a variety of disorders including stroke, Parkinson's disease, and Alzheimer's disease. Therefore, the possibility of enhancing neuroplasticity with external stimuli has far-reaching clinical implications including slowing age-related cognitive or motor decline.

One possible way to boost and sustain cognitive and motor performance in older adults is through the provision of specific motor and cognitive skills training programs. While there have been a few positive studies of brain training in older adults (Bamidis et al., 2014; Klingberg, 2010; Rebok et al., 2014), recent meta-analyses indicate that there is a lack of robust findings regarding the long-term efficacy and generalizability of such programs (George and Whitehouse, 2011; Martin et al., 2011; Papp et al., 2009). Moreover, there is renewed interest in the use of non-invasive brain stimulation (NIBS) techniques to modify cortical plasticity by means of extrinsic transient magnetic fields (i.e. passive modification rather than use- dependent modification). One technique in particular, transcranial direct current stimulation (tDCS), has enjoyed an extraordinary increase in popularity despite limited understanding of the neural mechanisms underlying the reported behavioural effects (de Berker et al., 2013).

tDCS involves the application of a weak electrical current (0.5–2 mA) continuously to the scalp via two surface electrodes (anode and cathode) for 10–20 min. Depending on the direction of current flow, tDCS can induce cortical excitability changes lasting for over 60 min following 15 min of stimulation (Nitsche and Fregni, 2007). Although there are a number of factors that may influence the response to tDCS (see Sections 4.2–4.5), anodal stimulation typically increases cortical excitability while cathodal stimulation decreases excitability. The neurobiological mechanisms underlying tDCS effects, however, are complex involving changes at multiple levels of description from the cellular level to modulation of the intrinsic network dynamics in the brain (Medeiros et al., 2012). Much of the knowledge regarding the physiological effects of tDCS has come from in vitro animal studies and pharmacological interventions in humans. Furthermore, somewhat different mechanisms appear to be involved in the cortical excitability changes evident during the period of stimulation and persistence of those changes following cessation of stimulation (Stagg and Nitsche, 2011).

1.1. During stimulation

The application of weak direct current stimulation (DCS) to the brain shifts the resting membrane potential of superficial horizontal intracortical interneurons resulting in changes to spontaneous neuronal excitability. Anodal stimulation increases neuronal firing rate through depolarization of resting membrane potentials whereas cathodal stimulation decreases firing rate and neuronal excitability through membrane hyperpolarization. Although the weak currents applied during stimulation do not evoke action potentials in a resting cell, recent in vitro research suggests that concurrent membrane potential changes in both the somata and axon terminals may underlie DCS-induced modulation of neuronal excitability (Rahman et al., 2013).

1.2. Stimulation after-effects

The transfer of the initial membrane potential shifts to longer-term modification of synaptic plasticity seem to involve processes similar to long-term potentiation (LTP) and long-term depression (LTD) through the modulation of NMDA receptors (Stagg and Nitsche, 2011). Pharmacological evidence indicates that tDCS elicits modifications in NMDA receptors via changes in post synaptic intracellular calcium concentration (Nitsche et al., 2003). There is strong evidence that in addition to influencing synaptic plasticity through modulation of glutametargic (NMDA and AMPA) receptors, the