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The effect of anodal transcranial direct current stimulation on motor sequence learning in healthy individuals: A systematic review and meta-analysis

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ABSTRACT

A large number of studies have indicated the effect of anodal transcranial direct current stimulation (a-tDCS) on the primary motor cortex (M1) during motor skill training. The effects of a-tDCS on different stages of motor sequence learning are not yet completely understood. The purpose of this meta-analysis was to determine the effects of single and multiple sessions of a-tDCS on two different tasks: the sequential finger tapping task/serial reaction time task (SEQTAP/SRTT) and the sequential visual isometric pinch task (SVIPT). We searched electronic databases for M1 a-tDCS studies. Thirteen studies met the inclusion criteria. The results indicate that application of multiple sessions of a-tDCS, compared to single session a-tDCS induced a significant improvement in skill in both SEQTAP/SRTT and SVIPT. Retention after a single day and multiple days of a-tDCS was statistically significant for the SEQTAP/SRTT task but not for SVIPT. Therefore, our findings suggest that application of M1 a-tDCS across the three or five consecutive days can be helpful to improve motor sequence learning.

1. Introduction

Motor sequence learning is defined as an inherent ability in humans to learn sequential actions, which has essential role in everyday life. This ability help us to learn numerous human skills from simple tasks such as pressing a button to complex activities like playing a piano (Keele, Ivry, Mayr, Hazeltine, & Heuer, 2003). Sequence motor learning can be categorized into two groups: explicit and implicit. In explicit motor sequence, learning occurs with awareness of sequential ordering of stimuli while in implicit motor sequence learning participants are not aware of this sequential ordering (Robertson, 2007).

A number of tasks have been developed to investigate different aspects of motor sequence learning. A frequently used paradigm is serial reaction time task (SRTT) in which participants respond to visual cue that appeared in one of four horizontal locations on a computer screen by pressing a key that corresponded to the stimulus locations (Keele et al., 2003; Robertson, 2007). Another commonly used task is sequential finger tapping task (SEQTAP) in which participants respond to a series of numbers from 1 to 4 displayed on a computer screen by pressing the corresponding button with the corresponding finger (Walker, Brakefield, Morgan, Hobson, & Stickgold, 2002). Another paradigm have been used to assess learning a sequence of forces is visual isometric pinch force task (SVIPT), in which participants learn how to control precisely their fingertip forces in a sequenced order of different target forces. Changes in movement speed, accuracy as well as skill, which are measured by combination of both speed and accuracy, could be considered as behavioural outcome measures to monitor improvement following motor sequence tasks.

In contrast to motor sequence learning, sensory-motor adaptation is the trial-and-error process of adjusting movement to new demands in which participants learn how to adapt a known movement to individuals or environmental changes such as driving a new car, adapting to perturbation caused by altered visual feedback on a computer screen or adapting to physical changes following an injury (Hill, Davey, & Kennard, 2000; Penhune & Steele, 2012). Therefore, performance improvements in motor adaption tasks occur as participants learn to return to a former level of performance whereas in motor sequence learning tasks, a higher level of skill acquired.

Improvement in outcome measures of motor learning can be occurred during training (online) but also after the training has

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ended (offline). Online and offline skill gains can be retained over time, resulting in long-term retention (Romano, Howard, & Howard, 2010). Therefore, motor sequence learning is characterized by fast and slow stages of learning. Fast learning occurs early on, within a single training session, and slow stage learning occurs later, in which incremental gains are achieved over multiple sessions of practice (Dayan & Cohen, 2011).

In the process of motor sequence learning, the functional properties of different brain areas can change as a result of practice and experience (Karni et al., 1998). Animal (Rioult-Pedotti, Friedman, & Donoghue, 2000) and human studies (Rosenkranz, Kacar, & Rothwell, 2007; Stefan et al., 2006; Ziemann, Ilic, Pauli, Meintzschel, & Ruge, 2004) have shown a strong link between motor learning and brain neuroplasticity. The process of motor skill learning involves the strengthening of synaptic connectivity. Long-term potentiation (LTP) has been identified as the likely physiological basis of learning (Rioult-Pedotti, Friedman, & Donoghue, 2000; Stefan et al., 2006; Ziemann et al., 2004). Depending on the task and the learning phase, different brain regions are engaged (Dayan & Cohen, 2011; Doyon & Ungerleider, 2002; Karni et al., 1998). One area of the brain, which is engaged in motor learning, is the primary motor cortex (M1) (Classen, Liepert, Wise, Hallett, & Cohen, 1998; Karni et al., 1995; Nudo, Milliken, Jenkins, & Merzenich, 1996; Pascual-Leone et al., 1995). This area has a crucial role in acquisition and consolidation of motor learning (Muellbacher et al., 2002; Nitsche et al., 2003).

Imaging studies demonstrated that M1 is differentially modulated during fast and slow stages of learning (Dayan & Cohen, 2011; Floyer-Lea & Matthews, 2005). There is no consensus on the activity of M1 during the fast or early stage of motor learning. Some studies showed decreased M1 activity (Downs & Black, 1998; Doyon & Ungerleider, 2002; Toni, Krams, Turner, & Passingham, 1998), while other researches showed increased activity. A number of studies did not show any changes in the activity of M1 in this phase (Downs & Black, 1998; Toni et al., 1998). In contrast to the fast stage of motor learning, there is a consensus on increased activation of M1 during the slow phase of learning (Dayan & Cohen, 2011; Floyer-Lea & Matthews, 2005; Karni et al., 1998). Due to the role of plastic changes in the cortical areas of the brain during motor skill learning (Pascual-Leone, Grafman, & Hallett, 1994; Pascual-Leone et al., 1995), non-invasive neuromodulatory techniques hold promise for enhancement motor learning through changes in corticospinal excitability (CSE).

Transcranial direct current stimulation (tDCS) is a safe and non-invasive technique to modulate CSE in a polarity-dependent manner (Nitsche et al., 2008; Priori, Berardelli, Rona, Accornero, & Manfredi, 1998). Anodal-tDCS (a-tDCS) leads to increased CSE (Nitsche & Paulus, 2000), while cathodal tDCS (c-tDCS) may results in decreased CSE (Nitsche et al., 2008; Priori et al., 1998). In a number of studies, a-tDCS was applied over M1 to boost the effects of training during variety of task paradigms such as SRTT (Kang & Paik, 2011; Kantak, Mummidisetty, & Stinear, 2012; Nitsche et al., 2003), SEQTAP (Kantak et al., 2012; Saucedo Marquez, Zhang, Swinnen, Meesen, & Wenderoth, 2013; Tecchio et al., 2010), SVIPT (Reis et al., 2009; Saucedo Marquez et al., 2013; Schambra et al., 2011), adaptation tasks (Kaski, Quadir, Patel, Yousif, & Bronstein, 2012), tracking tasks (Prichard, Weiller, Fritsch, & Reis, 2014) as well as other tasks such as Jebsen–Taylor Hand Function (Butts, Kolar, & Newman-Norlund, 2014).

Regarding to task specific effect of a-tDCS on motor learning (Saucedo Marquez et al., 2013), we focus on motor sequence tasks in this systematic review and meta-analysis. Although beneficial effects of a-tDCS over M1 for improvement of motor sequences have been identified (Cuypers et al., 2013; Nitsche et al., 2003; Reis et al., 2009; Saucedo Marquez et al., 2013; Schambra et al., 2011; Vines, Cerruti, & Schlaug, 2008; Vines, Nair, & Schlaug, 2008), the exact nature of involvement of M1 during application of single and multiple sessions a-tDCS at different stages of motor sequence learning is not yet understood. Therefore, the aim of this systematic review and meta-analysis was to investigate the effects of M1 a-tDCS on behavioural outcomes following single or multiple sessions of a-tDCS in both SEQTAP/SRTT and SVIPT.

2. Methods

2.1. Literature search

PubMed, Ovid Medline, Scopus, PROQuest, CINAHL, EMBASE, EBM reviews, Cochrane Library, Physiotherapy Evidence Database (PEDro) and SPORT Discuss were searched for appropriate studies published any time before February 2015. We also searched reference lists of all retrieved papers for additional references. Key search terms were: transcranial direct current stimulation, tDCS, non-invasive brain stimulation, corticospinal excitability, motor skill learning, motor sequence learning, transcranial magnetic stimulation, and TMS. This process identified 1708 articles and, after discarding duplicates, 1287 remaining articles were screened for suitability for inclusion in this meta-analysis.

2.2. Selection criteria

2.2.1. Inclusion criteria

Articles were included if they met the following criteria: (1) application of a-tDCS over M1, with conventional or other montages such as dual-hemisphere M1 stimulation or using an extra cephalic reference electrode, during motor sequence learning tasks; (2) having a control group (sham plus training or training only); (3) measurement of behavioural changes (such as movement speed, accuracy and skill) or CSE changes; (4) healthy individuals, and (5) published in peer-reviewed journals in English.

2.2.2. Exclusion criteria

In this systematic review, we focused on concurrent application of M1 a-tDCS during sequence motor learning tasks in upper limb. Therefore, we excluded articles if they applied a-tDCS during other tasks such as tracking tasks (Prichard et al., 2014), cognition tasks such as games, or adaptation tasks (Galea, Vazquez, Pasricha, Orban de Xivry, & Celnik, 2011; Hunter, Sacco, Nitsche, & Turner, 2009) and other tasks (Galea & Celnik, 2009; Minarik, Sauseng, Dunne, Berger, & Sterr, 2015). Studies that applied a-tDCS with a combination of therapeutic interventions, such as mental practice, motor imagery and pharmacological interventions (Kuo et al., 2008) were also excluded. Application of M1 a-tDCS before (Kuo et al., 2008) or after (Cantarero, Tang, O'Malley, Salas, & Celnik, 2013; Tecchio et al., 2010) motor sequence tasks were not included. Animal studies (Fritsch et al., 2010), reviews, case reports and letters were also excluded.

2.3. Quality assessment

Two researchers independently reviewed each included article and determined a quality score using the Physiotherapy Evidence Database (PEDro scale) (Moseley, Herbert, Sherrington, & Maher, 2002; Möcks, Gasser, & Tuan, 1984). The PEDro scale contains some items to assess the external and internal validity of the article, graded on a "yes/no" scale. The PEDro scale results in total scores from 0 to 10, with a higher PEDro score providing a surrogate indication of higher quality.