THE EFFECT OF ANODAL TRANSCRANIAL DIRECT CURRENT STIMULATION ON MULTI-LIMB COORDINATION PERFORMANCE

Abstract—Motor coordination is the combination of body movements performed in a well-planned and controlled manner based upon motor commands from the brain. Several interventions have been in practice to improve motor control. Transcranial direct current stimulation (tDCS) is getting a lot of attention these days for its effect in improving motor functions. Studies focusing on the ability of tDCS to improve motor control, inhibition and coordination are sparse. Therefore, the influence of tDCS stimulation at the right dorsolateral prefrontal cortex (DLPFC) on motor control and coordination was investigated, in a sham-controlled double-blinded pseudo-randomized design, with a multi-limb coordination task in healthy young subjects. Number of errors and reaction time were used as outcome parameters. Our findings showed that, anodal tDCS reduced the number of errors only in the heterolateral coordination condition, however there was no change in reaction time. No changes were found for the homolateral and three-limb coordination conditions. © 2015 IBRO. Published by Elsevier Ltd. All rights reserved.

Key words: tDCS, multi-limb coordination, motor control, inhibition.

INTRODUCTION

Motor coordination is the combination of body movements to perform functional, goal-directed actions. Intact motor coordination is essential for performing a variety of tasks such as tying a shoelace, reaching for a glass or walking; whereas, impaired motor coordination can greatly interfere with the execution of daily activities (Plotnik et al., 2011). As reported by Swinnen et al. (1997), motor control and motor coordination are subject to constraints (Swinnen et al., 1997), which are obvious in young children (Taub et al., 2004), elderly (Dutta et al., 2013) and patients with neurodegenerative diseases (Wu et al., 2007). These constraints differ from simple to complex, depending on the coordination and the phase (in-phase/anti-phase) in which the task is performed (Swinnen et al., 1995). Previously, it was demonstrated that two hands are constrained to act as one. Due to synergies of homologous muscles (Kelso et al., 1979) and the constraining factor experienced during movement of the ipsilateral limbs in opposite direction, which tends to reverse spontaneously to the ‘easy’ pattern i.e. same direction (Baldessar et al., 1982).

Constraints faced during coordination vary based upon temporal and spatial relationships between the effectors (Obhi, 2004). For example, in a complex bimanual coordination task, the phase relationship was studied by instructing subjects to draw a line with one hand and a circle with the other hand. Interestingly, the circle became more line-like and the line became more circle-like (Franz et al., 1991). This example illustrates that the phase relationship might shift from in-phase into anti-phase and vice versa (Swinnen and Carson, 2002). Two major constraint principles have been studied so far (Swinnen et al., 1997).

Firstly, the mirror-symmetrical movement with respect to midline has been termed the egocentric principle. Secondly, movements involving non-homologous effectors (i.e. an arm and leg) in the same direction are termed as allocentric principle. During multiple limb coordination, even more complex combinations of these basic constraints will be presented. Moreover, the basic constraints that are inherent to the control of coordination patterns become apparent, when different movements have to be performed simultaneously with multiple limbs (Swinnen, 2002). Previous work provided evidence that, exercise therapy in both healthy and patient populations can improve motor coordination by optimizing motor control and inhibition (Swinnen and Carson, 2002; Wu et al., 2007; Harrison et al., 2013). However, to our knowledge, there are currently no alternatives available to further improve motor coordination.

Recently, transcranial direct current stimulation (tDCS), a non-invasive brain stimulation technique, has shown to be capable of optimizing motor performance in...
prior to inclusion, subjects were screened for TMS/tDCS and injection of the prefrontal cortex regarding the motor functions are sparse, recent evidence indicated that the right DLPFC is considered as a key region for executive motor control (Cieslik et al., 2013). Furthermore, the dominance of the right DLPFC in monitoring operations and conflict resolution during motor response execution is also supported by other studies (Aron et al., 2003, 2004; Shallice, 2004; Nee et al., 2007; Vogt et al., 2007). Additionally, evidence from functional magnetic resonance imaging indicated that the right dorsal prefrontal region plays a prominent role in integrating response inhibition and execution of appropriate action commands (Garavan et al., 1999). Until now, there are no studies reporting the effects of atDCS stimulation of the right DLPFC on motor control during multiple limb coordination. As atDCS was found to have an effect in performance mainly by improving motor inhibition (Boggio et al., 2007), the current study aimed to investigate the potential use of atDCS in the inhibition of motor constraints through cognitive action control during multiple limb coordination. Moreover, we hypothesize that tDCS inhibits the constraints and consequently improves multiple limb coordination.

EXPERIMENTAL PROCEDURES

Subjects

Prior to inclusion, subjects were screened for TMS/tDCS contra-indications (Wassermann, 1998) as well for exclusion criteria. Subjects were excluded from the analysis if they were left-handed, performed the task without mistakes at the baseline (ceiling effect) and/or if they reported alcohol or caffeine intake the day prior to the experiment. Finally, 39 subjects (21 men and 18 woman) aged between 18 and 35 years (mean: ±20.3 years; standard deviation: ±1.9) participated in this double-blinded, pseudo-randomized study. All subjects had normal or corrected-to-normal vision. Subjects were provided written informed consent; and the central ethics committee of the UZ Leuven and the local ethics committee of the University of Hasselt approved the experimental procedures. The study complies with the principles stated in the Declaration of Helsinki.

Experimental design

The experiment was performed in two groups. The experimental group (n = 19; 12 males, seven females) received atDCS and the control group (n = 20; nine males, 11 females) received sham tDCS (stDCS). Both groups were asked to perform an identical motor task consisting of different coordination patterns. To make sure all subjects understood the goal of the task, a 2-min familiarization session was provided prior to the experiment. Next, motor performance was measured for ±5 min (baseline), followed by the intervention (atDCS or stDCS), which lasted 20 min. During the last 5 min of the stimulation motor performance was measured again (see Fig. 1).

Non-invasive brain stimulation

The subjects received either atDCS or stDCS. As the right DLPFC was found to play a prominent role in cognitive control of motor behavior (Aron et al., 2003, 2004; Shallice, 2004; Nee et al., 2007; Vogt et al., 2007; Cieslik et al., 2013), the anode (surface 25 cm²) was placed over the right DLPFC (according to the method of DaSilva et al. (2011)) and the cathode (surface 35 cm²) over the left contralateral supraorbital region. To minimize possible side effects under the cathode, this electrode was increased to make it more functionally inert (Nitsche et al., 2007). In order to avoid the effect of current shunting through the skin, the two electrodes were positioned at least 8 cm apart from each other (DaSilva et al., 2011). The stimulation group received atDCS for 20 min at an intensity of 2 mA. Exactly the same set-up was used in the sham group, with the difference that they only received atDCS during the first 60 s (30 s of ramp up and 30 s of ramp down).

Motor task

We used a multi-limb task to study the effect of atDCS on motor coordination. Subjects were seated in front of a 2, 3
PC-screen with their hands and feet resting on tablets with capacitive switches (Pepperl Fuchs CBN5-F46-E2, sampling frequency: 1000 Hz, Mannheim, Germany). Four squares corresponding with the four limb segments were presented on the PC-screen (see Fig. 2A). The squares turned white if all the limbs were in contact with the tablets (see Fig. 2B). After two seconds, the squares turned randomly blue in different combinations. Subjects were instructed to raise their limbs as fast and as accurately as possible, corresponding to the visual stimulus. For example, if both squares on the right hand side turned blue, subjects should raise their right hand and right leg. If the task was performed correctly, the blue squares presented on the screen turned green. If a non-requested limb was raised, the corresponding square turned red, indicating an error. Eight different combinations (see Fig. 2C) of visual stimuli based upon the constraints (Swinnen et al., 1997) were presented in this experiment. All eight combinations were repeated eight times in a fully randomized order. Accuracy (number of errors) and speed (change in reaction time) were measured to assess the performance.

Data analysis

The effect of atDCS vs. stDCS on response inhibition to motor constraints was assessed using the parameters, change in reaction time (RT) which is defined as RT at baseline – RT during the last 5 min of the stimulation and the difference in the number of errors (number of errors baseline – number of errors during the last 5 min of the stimulation). The number of errors is defined as the total number of errors over all trials divided by the number of trials, which represents the average number of errors per trial (ANE).

The movement coordination patterns were analyzed in clusters based upon the number of limb movements and the corresponding constraints (see Table 1). This resulted in three clusters: (1) homolateral coordination (combination-1: right-hand + right-leg; combination-2: left-hand + left-leg), (2) heterolateral coordination (combination-1: right-hand + left-leg; combination-2: left-hand + right-leg) and (3) three-limb coordination (combination-1: right-hand + right and left-leg; combination-2: left-hand + right and left-leg; combination-3: right and left-hand + right leg; combination-4: right and left-hand + left-leg). RT was analyzed in two parameters [fastest RT (FRT), mean RT (MRT)] in milliseconds. The FRT was calculated based upon the fastest reaction time among all trials per combination. The MRT was calculated based upon the mean of the reaction time of all trials per combination and also includes the amount of time spent in making errors. A general linear model, modeling the difference between baseline and post-intervention performance as a function of treatment, baseline performance and (if necessary) the interaction, was applied (SAS v9.2). More specifically, the following model was used: \[
\text{diff} = \text{baseline} + \text{trt} + (\text{baseline} / C2)\text{trt},
\]
where ‘diff’ is the difference between the baseline and the post-intervention performance, ‘baseline’ represents the baseline performance and ‘trt’ represents the treatment with either atDCS or stDCS. The significance level was set at \(p < 0.05\). Normality and homoscedasticity of the data were checked by the Shapiro–Wilk and Levene’s test, respectively and an outlier analysis was performed to investigate consistency of results.

Fig. 2. Overview of movement combinations and multi-limb coordination task performance. (A) The experimental set-up and the response of the subject to a heterolateral movement combination. (B) The visual response was presented in the form of four squares connected with four tablets. The four gray squares presented in the screen turned white once the limbs established good contact with the tablets. The blue squares turned green when there was correct response and when a non-requested limb was raised; the error was indicated by red squares. (C) Subjects received a visual response as squares representing different movement combinations were grouped under, (1) homologous combinations (2) heterologous combinations (3) three-limb combinations. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)
Table 1. Average group data (± SD) for error reduction [average number of errors (ANE)], reaction time [fastest (FRT) and mean reaction time (MRT)] are shown corresponding to each movement combination. The error reduction [Δ (post-pre) atDCS – Δ (post-pre) stDCS] and the difference in reaction time [Δ (post-pre) atDCS – Δ (post-pre) stDCS] are also shown.

<table>
<thead>
<tr>
<th>Movement coordination patterns</th>
<th>Error reduction</th>
<th>Reaction time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ANE (total errors/trails)</td>
<td>FRT (ms)</td>
</tr>
<tr>
<td></td>
<td>atDCS</td>
<td>stDCS</td>
</tr>
<tr>
<td></td>
<td>Baseline Post</td>
<td>Baseline Post</td>
</tr>
<tr>
<td>Homolateral combinations</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.0098</td>
<td>0.0098</td>
</tr>
<tr>
<td>Heterolateral combinations</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.5921</td>
<td>0.273</td>
</tr>
<tr>
<td>Three–limb combinations</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.2648</td>
<td>0.199</td>
</tr>
<tr>
<td>All combinations (homolateral + heterolateral + three–limb)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.2829</td>
<td>0.1702</td>
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</tbody>
</table>

RESULTS

Group data and the corresponding p-values for the number of errors and change in reaction time are shown in Tables 1 and 2, respectively.

Accuracy (number of errors)
For the heterolateral limb coordination there was a significant effect of the intervention on ANE (p = 0.0074), but not for the homolateral limb coordination or the three-limb coordination (all, p > 0.05).

As mentioned above an outlier analysis was performed since three observations seem to deviate from the majority (Fig. 3) and can be considered as potential outliers. As such these observations can possibly influence the results and more importantly their influence might be in favor of the desired treatment effect. For this reason it was decided to investigate their impact by applying the same analysis separately for subsets of the total dataset removing every possible set of the above-mentioned outliers. Results of these analyses are shown in Table 3. It is clear that the final conclusion with respect to the treatment effect is not changing.

Speed (reaction time)
The reaction time was analyzed using FRT and MRT. There was no significant effect of the intervention on change in FRT or MRT for homolateral limb coordination, heterolateral limb coordination or the three-limb coordination (all \(p > 0.05\)).

DISCUSSION
This is the first study that aimed to investigate the effect of atDCS on motor control and coordination in healthy subjects. Although, it was expected that atDCS would lead to improved performance in different (homolateral, heterolateral and three-limb) coordination conditions, only a significant reduction in the number of errors in the heterolateral condition was found. More specifically, it was previously documented that bilaterally symmetric movements, which required simultaneous activation of homologous muscles, were more accurate and consistent than asymmetrical movements involving non-homologous muscles (Swinnen and Carson, 2002). While performing three-limb coordination patterns, the subject had to inhibit more than one constraint, the homologous muscle constraint which was probably the strongest constraint together with the ipsilaterally and heterolaterally isodirectional constraints (Meesen et al., 2006). In the three-limb coordination patterns subjects had to inhibit the movement of one limb, which was subject to the mentioned constraints. In the two-limb heterolateral

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Table 2. General linear model. Type 3 tests for fixed effects are shown for each movement combination for error reduction [average number of errors (ANE)], reaction time [fastest (FRT) and mean reaction time (MRT)]. The following model was used: \(\text{diff} = \text{baseline} + \text{trt} + (\text{baseline} \times \text{trt})\), where ‘diff’ is the difference between the baseline and the post-intervention performance, ‘baseline’ represents the baseline performance and ‘trt’ represents the treatment with either atDCS or stDCS.

<table>
<thead>
<tr>
<th>Movement coordination patterns</th>
<th>Type 3 fixed effects</th>
<th>Error reduction</th>
<th>Reaction time</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>ANE</td>
<td>FRT</td>
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<tr>
<td></td>
<td></td>
<td>F-Value</td>
<td>p-Value</td>
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<tr>
<td>Homolateral combinations</td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td>trt</td>
<td>0.92</td>
<td>0.3451</td>
</tr>
<tr>
<td></td>
<td>base</td>
<td>79.26</td>
<td>&lt;0.0001</td>
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<tr>
<td></td>
<td>base × trt</td>
<td>0.06</td>
<td>0.8113</td>
</tr>
<tr>
<td>Heterolateral combinations</td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>trt</td>
<td>0.02</td>
<td>0.8926</td>
</tr>
<tr>
<td></td>
<td>base</td>
<td>26.58</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>base × trt</td>
<td>8.09</td>
<td>0.0074</td>
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<tr>
<td>Three-limb combinations</td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>trt</td>
<td>0.00</td>
<td>0.9677</td>
</tr>
<tr>
<td></td>
<td>base</td>
<td>43.00</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>base × trt</td>
<td>2.48</td>
<td>0.1246</td>
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</table>
In contrast to the reduction in the number of errors, Growing amount of literature evidence shows that tDCS facilitates a variety of functions such as working performance. This implies that subjects might have been focused primarily on the improvement of their performance level in context of reduction of errors during performance. Growing amount of literature evidence shows that tDCS facilitates a variety of functions such as working memory, force control and reaction time (Jo et al., 2009; Reis et al., 2009; Keenser et al., 2011; Ferrucci and Priori, 2013). These findings support our finding that tDCS reduced the number of errors in heterolateral coordination condition. More specifically, atDCS stimulation on the DLPFC region was found to improve the response inhibition during the performance of the go-no-go task (Boggio et al., 2007).

Table 3. Outlier analysis. The same data analysis was performed to analyze the impact of outliers separately for subsets of the total dataset removing every possible set of outliers. The “trt” indicates ‘treatment’; “ANE.pre.hetero” represents the baseline of the average number of errors in the heterolateral combination.

<table>
<thead>
<tr>
<th>Effect</th>
<th>p-Values</th>
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<tbody>
<tr>
<td>All data</td>
<td>A</td>
</tr>
<tr>
<td>trt</td>
<td>0.8926</td>
</tr>
<tr>
<td>ANE_pre_hetero</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>ANE_pre_hetero * trt</td>
<td>0.0074</td>
</tr>
</tbody>
</table>

To summarize, we can conclude that atDCS significantly improved heterolateral motor coordination with respect to reduction of errors. Unfortunately, atDCS did not result in improved performance for the homolateral and the three-limb coordination conditions.

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REFERENCES


CONCLUSION

To summarize, we can conclude that atDCS significantly improved heterolateral motor coordination with respect to reduction of errors. Unfortunately, atDCS did not result in improved performance for the homolateral and the three-limb coordination conditions.


