

## MASTERPROEF DEEL 2

'THE INFLUENCE OF BIHEMISPHERIC ANODAL TDCS ON THE  
PERFORMANCE OF A SWITCHING TASK IN MS PATIENTS'

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## **Acknowledgement**

This article is situated in our second master Science of rehabilitation and kinesitherapy at the University of Hasselt (Belgium). The aim of our article was to examine the effects of tDCS in MS patients. Firstly we would like to thank our promotor, Prof. Dr. R. Meesen, for instructing and guiding us in the literature search and assisting us when needed. Secondly we would like to thank Dra. D. Leenus for the aid in the literature search and for the set-up of the experiment. Finally, special thanks to family for the support during the writing of the article and in particular A. Reynders for assisting us with the statistical analysis.

## **Research framework**

This study is part of a wider research under the lead of prof. Dr. R. Meesen and Dra. D. Leenus of the university of Hasselt. In fact, it is part of the doctoral study of Daphnie Leenus (“Does bi-hemispheric tDCS ameliorate motor control and coordination in MS patients?”) under the project: “Does tDCS improve the motor functions and abilities of MS patients?” (R-3010). It is funded by the Special Research Fund (BOF) of the University of Hasselt. The experiment was conducted in the ‘MS- en revalidatiecentrum’ in Overpelt (Limburg). As part of a threefold experiment, it is confined to investigate the effect of tDCS in multiple sclerosis (MS) patients on a switching task. Both students helped with the execution of the experiment under supervision of Dra. Leenus. The research design and method was premised by prof. Dr. Meesen and Dra. Leenus.

Transcranial direct current stimulation (tDCS), a non-invasive brain stimulation technique, has been proven to be effective in a variety of populations. It has led to many positive results in the research of the rehabilitation of several neurodegenerative disorders. However, the effect of tDCS in patients with multiple sclerosis is scarcely explored.

In this study we investigated the effect of tDCS on MS patients while performing a switching task, this is a multilimb task combined with a cognitive component. Literature points out that several cognitive and motor processes in MS patients are impaired and therefore these patients experience all kinds of problems in daily life activities. Because eventually, making decisions about a following motor action and performing motor tasks are processes the human being is constantly challenged with.

In this switching task, participants had to make a choice between two possible kinds of motor reactions and afterwards they had to perform these motor actions in a correct manner. In a way, this task resembled activities of the daily live. An example of when this situation occurs is when one is standing in front of a traffic light that has turned green and consequently one has to change gears in the correct manner.

The experimental set-up was mainly based on the set-up used in a former study conducted by D. Leenus et al. (2015) (Leenus, Cuypers, Vanvlijmen, & Meesen, 2015).



## **Abstract**

### Objective

The aim of this study is to look into the potential use of atDCS (anodal tDCS) and its influence on motor control while performing a switching task.

### Methods

In total eleven participants were recruited. They received bi-hemispheric anodal or sham tDCS over the primary motor cortex (M1). Meanwhile, the participants performed a switching task. A double blinded, pseudo-randomized, cross-over design was used (group A: stimulation group, group B: control group). The primary outcome was the performance of the switching task (accuracy and reaction time).

### Results

Our results showed that the participants receiving stimulation A made more errors and had an increased reaction time. Over time, stimulation A showed a small but not significant positive effect on the total error rate. Reaction time on the other hand, was significantly decreased over time when receiving stimulation A.

### Conclusion

The application of tDCS could be favorable during motor learning in MS patients, leading to improved reaction times and to a lesser extent to a reduction of errors.

### Keywords

Multiple sclerosis, primary motor cortex, transcranial direct current stimulation, reaction time, switching task.



## 1. Introduction

Multiple sclerosis (MS) is an autoimmune disease that affects the brain and spinal cord, resulting in loss of motor control, vision, balance and sensation (Kingwell et al., 2013). Besides this, MS also affects cognition, thereby leading to a slowdown in several cognitive processes like decision-making, mental processing speed, memory and executive functions (Benedict et al., 2011)

Because of the impairment in corpus callosum (CC) structures, the coordination involving multiple limbs is one of the first aspects to deteriorate. These connectivity abnormalities of the CC cause a disruption of interhemispheric pathways and therefore impair the inhibition and facilitation processes (Wahl et al., 2011). Since in MS-patients several cognitive processes are delayed (Benedict et al., 2011), they experience problems with cognitive action control. This process is essential to perform motor tasks as quickly and accurate as possible.

Recently, transcranial direct current stimulation (tDCS), a non-invasive brain stimulation technique, has been proven to be an effective tool in neurorehabilitation (Boggio et al., 2007; Stagg et al., 2011). It is capable of improving motor performance in healthy subjects and in patients with neurodegenerative disorders (Cuyppers, Leenus, van den Berg, et al., 2013; Meesen, Thijs, Leenus, & Cuyppers, 2014). As per the existing scientific studies, the effects of tDCS on cognitive action control have never been investigated in MS patients. In healthy participants, however, while performing a switching task, there was a significant switch cost in reaction time when comparing non-conflicting trials and conflicting trials (Mennigen et al., 2014). Previous research of Pohl et al. (2006) demonstrates that subjects with stroke had significant higher switch costs than control subjects for accuracy (Pohl et al., 2007). There was no difference in reaction time switch costs.

A large number of studies have examined the effects of stimulation of specific cortical areas, like the primary motor cortex (M1) (Bastani & Jaberzadeh, 2013; Cuyppers, Leenus, Van Wijmeersch, et al., 2013; Kidgell, Goodwill, Frazer, & Daly, 2013). According to Nitsche et al. (2003), unilateral anodal stimulation of the M1 resulted in increased performance in a simple motor task (Nitsche et al., 2003). Boros et al. (2008) found a decrease in intracortical inhibition and an increase of intracortical facilitation after the application of anodal tDCS on M1 in healthy participants (Boros, Poreisz, Munchau, Paulus, & Nitsche, 2008). Recently, Leenus et al. (2015) investigated the effect of atDCS stimulation at the right dorsolateral prefrontal cortex (DLPFC) on motor control and coordination in healthy subjects (Leenus et al., 2015). They concluded that anodal tDCS on the right DLPFC has an effect on the number of errors only in a heterolateral coordination condition, while no change in reaction time was found. The protocol of this experiment was partially based on this study. The switching task that was performed, has similar characteristics to the task used by Leenus et al. (2015) (Leenus et al., 2015).

Few studies report bi-hemispheric anodal tDCS, none have investigated effects in MS patients. Gomes-Osman et al. (2013) performed a bi-hemispheric anodal tDCS study in healthy participants, in which the participants performed a bimanual typing task while receiving stimulation over the corticomotor hand areas (Gomes-Osman & Field-Fote, 2013). The results show a positive influence on bimanual skilled hand performance. Studies that applied anodal tDCS on one hemisphere and cathodal tDCS on the contralateral hemisphere, however, have been performed frequently. Leite et al.

(2013) performed an experiment where bi-hemispheric tDCS was applied (anodal and cathodal) while healthy subjects performed a switching task (Leite, Carvalho, Fregni, Boggio, & Goncalves, 2013). The results show that left anodal tDCS improved switching performance, right anodal tDCS improved accuracy of the task.

To our knowledge, there are no studies investigating the effects of bi-hemispheric atDCS of the primary motor cortex in MS patients. The aim of this study was to look into the potential use of atDCS and its influence on motor control while performing a switching task. Since a cognitive component is added, we hypothesize that bi-hemispheric atDCS improves cognitive action control in MS participants.



## 2. **Methods**

### 2.1. Subjects

Participants were recruited from the 'MS- en revalidatiecentrum' in Overpelt (Limburg). Twenty relapsing remitting MS patients agreed to participate in this study. Five participants were excluded based on the exclusion criteria. Four participants dropped out (two of them suffered a fracture of the lower limb, one participant experienced the study as too exhausting and one participant suffered from low back pain). Eventually, eleven participants (seven women, four men) completed the study. The participants were between 18 and 65 years old. EDSS scores varied between 1.5 and 4.5. Detailed info concerning the participants can be found in table 1. Patients completed a general questionnaire concerning daily habits (employment, smoking, etc.) and use medication

Prior to the first session, the Oldfield Handedness Questionnaire was used to determine the handedness. Also the Mini Mental State Examination (MMSE) and the Symbol Digit Modality Test (SDMT) were used to determine the patient's cognitive abilities.

All participants were informed about the experimental procedures and gave their written informed consent. The experimental procedures were approved by Medical ethics committee of the University of Hasselt (UH) and the 'Katholieke Universiteit Leuven (KUL)'.

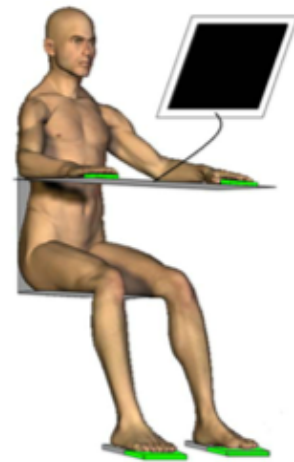
**Table 1.** Clinical Details for Multiple Sclerosis Participants

<b>Name</b>	<b>Gender</b>	<b>Age</b>	<b>EDSS score</b>	<b>Dominant hand</b>	<b>Most impaired</b>
Participant 1	M	35	3	L	R
Participant 2	M	60	4	R	R
Participant 3	F	46	2	R	R
Participant 4	M	61	2,5	R	R
Participant 5	F	45	1,5	R	R
Participant 6	F	38	3	R	R
Participant 7	M	59	1,5	R	R
Participant 8	F	46	4	R	R
Participant 9	F	69	2	R	R
Participant 10	F	24	2,5	R	R
Participant 11	F	49	2	R	R

### 2.2. tDCS of the primary motor cortex

Prior to inclusion, participants were screened for tDCS contra-indications (Wassermann, 1998). tDCS was delivered by a Newronika HDC stimulator via saline-soaked surface sponge electrodes. Participants received bi-hemispheric anodal or sham tDCS over the primary motor cortex (M1). The placement of the electrodes was performed in a standardized way (Da Silva et al. 2011). The

localization was confirmed by a 10/20 EEG system. The anodal electrodes were placed bilaterally on the motor cortex, while the cathodal electrode was placed at the supra-orbital region. The electrodes were fixed with straps. In one session the participants received tDCS with an intensity of 1.5 mA ( $0.06\text{mA}/\text{cm}^2$ ), in the other session they received tDCS only for the first 30 seconds (30 sec ramp-up/ramp-down). The session in which the tDCS was applied, will be discussed as the 'stimulation group', the session in which sham tDCS (stDCS) was applied, will be discussed as the 'control group'.



**Fig. 1 and 2** Experimental set-up

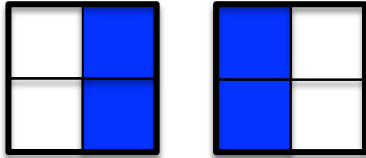
### 2.3. Motor task

While receiving tDCS, participants performed a switching task that demanded the involvement of all four limbs. Therefore it was very similar to the task that was described by Leenus et al. 2015. In this task, participants were seated in front of a computer screen with their hands and feet placed on a touch-sensor (figure 1 and 2). Four grey squares were visible on the screen, which represented the four limbs. Subjects had to lift their limbs concordant with the blue stimuli that were shown on the screen (figure 3). For example, when both left squares turned blue, participants had to lift their left hand and their left foot. Participants were encouraged to perform the task as fast as possible, but with as few errors as possible.

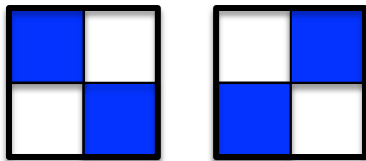
The difference with our task was the addition of a cognitive component, and therefore increasing the difficulty. In this switching task program, prior to the stimulus, a visual cue was shown (pre-cue). Following this pre-cue, participants had to adapt their response. There were two possible pre-cues, namely a green one or a red one. Consequently, there were two possible responses. When the green pre-cue was shown, participants had to perform the task concordant with the blue stimuli shown. However, when the red pre-cue was shown, they had to inhibit this reaction and give the opposite response i.e. not responding to the blue squares, but to the other squares. Therefore one must be able to inhibit a prior learned motor task set while activating a new learned task set. One of the parameters to describe cognitive-action control is a term called switch cost (see Discussion). This is mostly an increased mean reaction time (RT) or error rate (ER) between the non-conflicting trial (in our

task: green switch cue) and the conflicting trial (red switch cue). A conflicting trial is a trial to test the participant's cognitive-action control.

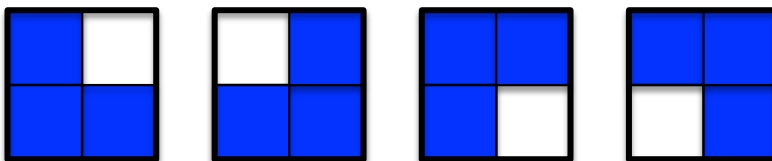
### Homolateral combinations



### Heterolateral combinations



### Three-limb combinations

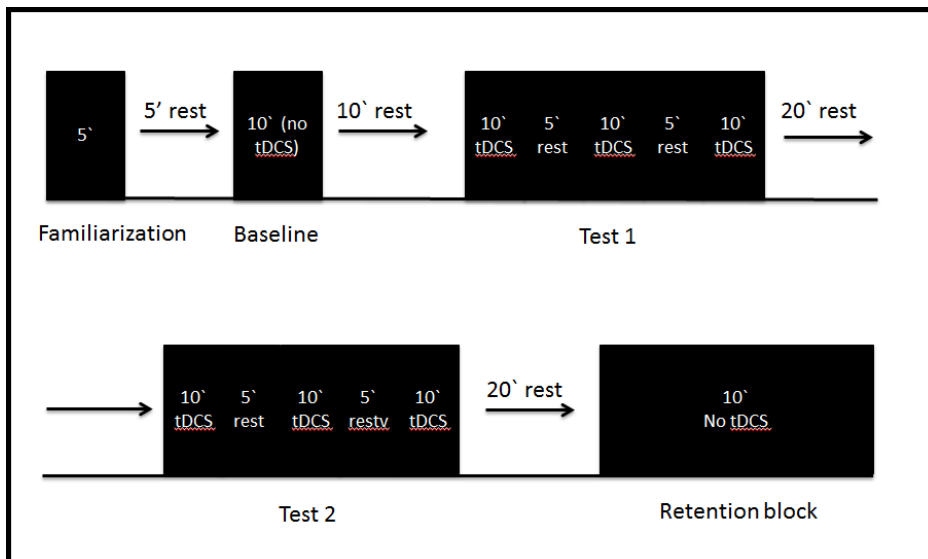


**Fig. 3.** Overview of all possible movement combinations

#### 2.4. Experimental procedures

The study was conducted using a double blinded, pseudo-randomized, cross-over design. The experimental sessions were separated by at least 48 hours to avoid carry-over effects. The experiment was performed in two sessions in which the participants received either repetitive bi-hemispheric anodal or sham tDCS. Each session consisted of a familiarization (5min), a baseline measurement, two intervention sessions and a retention block (see figure 4).

During the familiarization, participants became acquainted with the task. During the five minutes of rest in between, the localization of the electrodes was determined. After the baseline measurement, there was a 10 minute rest period in which the tDCS electrodes were positioned. Subsequently, the participants performed the first test battery for about 30 minutes with tDCS. After each ten minutes of stimulation there was a rest period of five minutes. Before performing the second test battery, there was a 20 minute break. Finally, participants performed the retention block without receiving tDCS.



**Fig. 4.** Time-line of one tDCS session

VAS-scores were assessed six times during each session, namely before baseline, after the first test battery, before and after the second test battery and before and after the retention block. The parameters which were scored were attention, fatigue, pain, quality of sleep, stress and feeling sickness.

## 2.5. Data management and statistical analysis

**The primary outcomes** were Accuracy (total number of errors) and Reaction Time of the switching task. These outcomes were analyzed per movement combination. There were three possible movement combinations: homolateral, heterolateral and three-limb combinations. The results were analysed with a generalized linear model and fitted with the glimmix procedure by Prof Thijs (Censtat UHasselt). **Secondary outcomes** were Sleep quality, Stress, Attention, Fatigue, Feeling Sickness and Pain. These outcomes were measured by a VAS-scale. For analyzing the VAS scores, t-tests were performed by using the program SAS JMP.

### 2.5.1. VAS scores

A parametric or non-parametric t-test (if the data were not normally distributed) was performed to analyze the VAS scores, a Bonferroni correction was used to counteract for repeated measures. Therefore the level of significance was set at  $p = 0.0083$ . Since this is a rather strict measure, a post-hoc power analysis was performed when p-values were between 0.0083 and 0.05. If the power was 80% or higher, this was still considered as a significant result.

There was also searched for correlations between the parameters. These correlations are described in tables 2 and 3.

**Table 2.** Correlations between the parameters of stimulation A

Correlation stim A	Pre		Post	
	Sleep quality	Fatigue	Sleep quality	Fatigue
Fatigue	0,8625		0,8363	
Attention	0,7145	0,8225	0,8462	0,8701
Stress	(abnormal distribution)		-0,0831	
Pain	-0,1632		0,1775	
Feeling sick	0,5173		0,5491	

**Table 3.** Correlations between the parameters of stimulation B

Correlation stim B	Pre		Post	
	Sleep quality	Fatigue	Sleep quality	Fatigue
Fatigue	0,8624		0,8379	
Attention	0,8894	0,9561	0,8997	0,9022
Stress	-0,1775		-0,1304	
Pain	-0,4197		-0,3481	
Feeling sick	0,4185		0,6421	



### **3. Results**

#### **3.1. VAS-scores**

##### **3.1.1. Pre-Post**

In the stimulation group, there was a significant difference in fatigue, when comparing pre VAS scores with post VAS scores ( $p=0,0454$ ). Post-hoc power analysis revealed a power of 17%. Also for feeling sickness there was a significant effect ( $p=0,0356$ ) in the post-VAS scores compared to the pre-VAS scores post-hoc power was 27%. In the control group, there was a strong significant effect on attention in the post-VAS scores ( $p=0,0068<0.0083$ ).

##### **3.1.2. Pre VAS scores**

There was no significant difference in VAS score (for all parameters) when comparing the scores of both groups at the start of the session.

##### **3.1.3. Post VAS scores**

When comparing post VAS scores of the stimulation group (stimulation A) and the control group (stimulation B), one parameter differed significantly, namely stress ( $p=0.0020$ ). This value indicates more stress in the control group. Post-hoc power was 15%.

##### **3.1.4. Correlation**

A correlation was considered strong if a score was (-) 0.5 or higher (T. Vanhoornissen, 'Inductieve statistiek voor de gedragswetenschappen, toegepaste hypothesetoetsing met SPSS' (2012). In both pre- and post-measurements and in both sessions, a strong correlation was found between Sleep Quality and Attention, Sleep Quality and Fatigue and between Fatigue and Attention in both groups and in both pre- and post-measurements. Sleep Quality has a strong influence on Attention and Fatigue.

#### **3.2. Rate of success (number of errors)**

The heterolateral and 3-limb coordination condition showed a significant higher number of errors in comparison with the homolateral coordination condition ( $p<0.0001$ ). These two conditions were significantly less accurately executed. During the familiarization phase of the experiment, the participants receiving stimulation A, made more errors. Stimulation A over time showed a small, but not significant, positive effect on the total error rate ( $p=0.0731$ ). When comparing both switch cues, a significant difference ( $p=0.0086$ ) was seen. Namely the green pre-cue resulted in fewer errors compared to the red pre-cue.

#### **3.3. Reaction time**

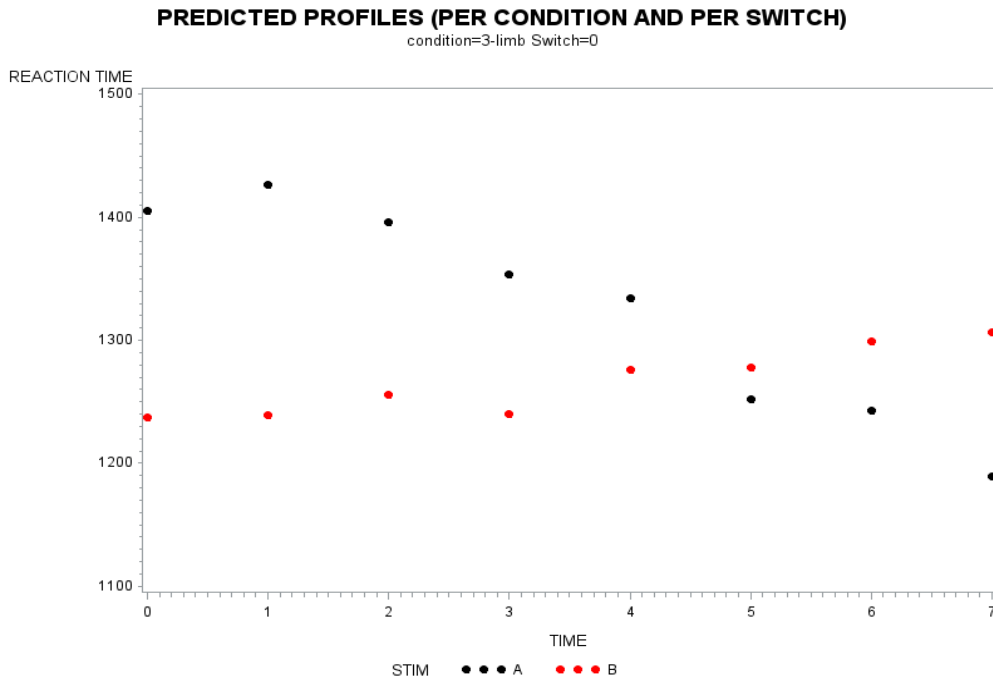
When comparing all three coordination conditions, less time was needed to react when a homolateral coordination condition was shown. Meanwhile, there was a significant increase in reaction time regarding the heterolateral ( $p<0.0001$ ) and three-limb coordination condition ( $p=0.0059$ ). At the start of

the experiment, the stimulation group (stimulation A) had significant higher reaction times ( $p=0.0145$ ). Over time stimulation A showed a significant decrease in reaction time.

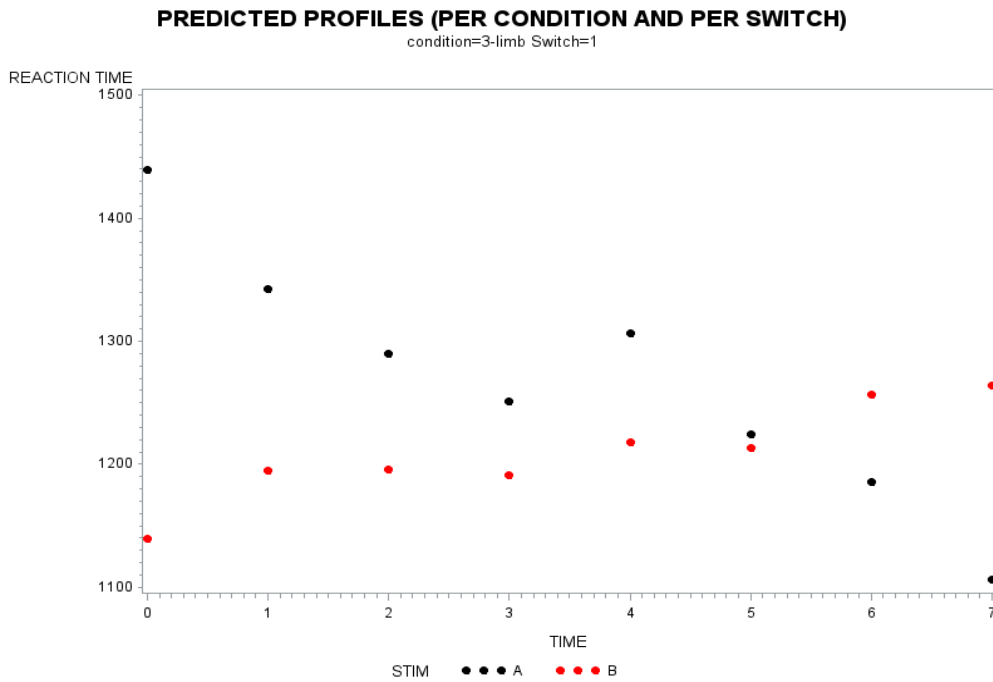
**Table 4.** Data for number of errors and reaction time. This is shown for all three conditions, both stimulation groups and both switch cues. The differences in reaction time over time in all three conditions (time \* condition) and the differences in number of errors and reaction time in both stimulation groups over time (time \* stimulation) are also shown.

	Number of errors		Reaction time	
	Estimate	P-value	Estimate	P-value
<b>Conditions</b>				
Three-limb combinations	- 0.8322	<.0001	442.97	0.0059
Heterolateral combinations	- 1.1024	<.0001	855.64	<.0001
Homolateral combinations	0	-	0	-
<b>Stimulation</b>				
A	-0.3659	<.0001	242.60	0.0145
B	0	-	-	-
<b>Time * condition</b>				
Three-limb combinations			-36.5039	0.1975
Heterolateral combinations			-78.5836	0.0196
Homolateral combinations			0	-
<b>Time * stimulation</b>				
A	0.07849	0.0731	-50.4415	0.0352
B	0	-	0	-
<b>Switch</b>				
Green	0.1268	0.0086	49.1964	0.3647
Red	0	-	0	-

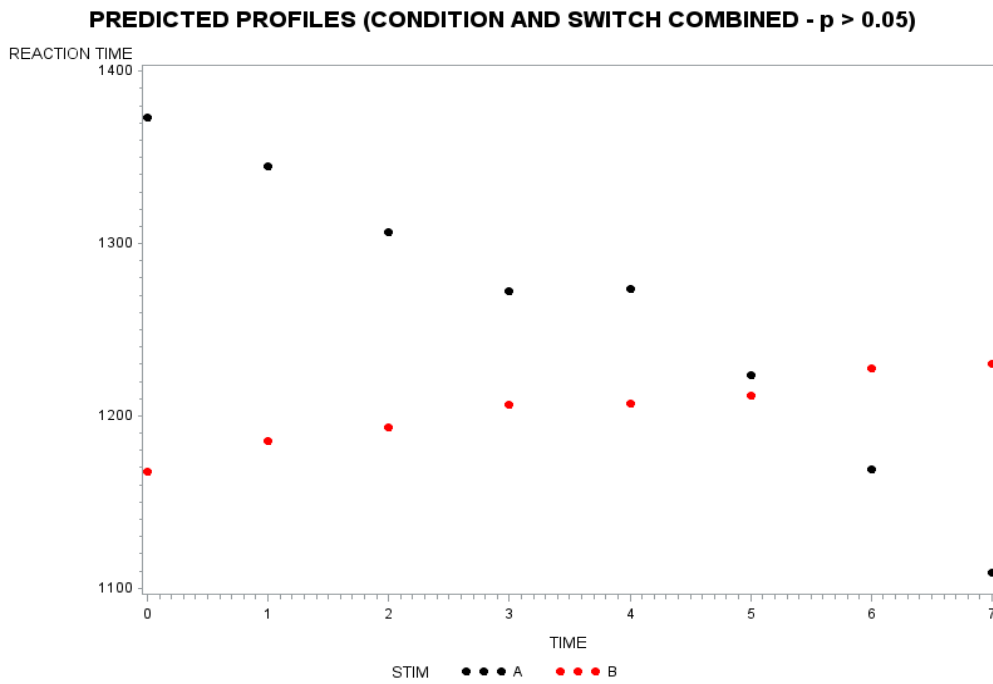




**Fig. 5** This figure shows the difference in reaction time between both groups (stim. A and B) when performing the 3-limb combination condition preceded by the green switch cue from the beginning of the experiment until the end. Initially, the stimulation-group (stim. A) had higher reaction times in comparison with the control-group. But throughout the experiment, the reaction time of the stimulation group decreased while it slightly increased in the control-group.



**Fig. 6** The difference between both groups (stim. A and B) is shown when performing the same coordination condition as in figure 4, but here it was preceded by the red switch cue. We can conclude that there is little difference in reaction time between the green and the red switch cue.



**Fig. 7** General overview of the difference in reaction time between stimulation-group and control-group from beginning to end. Initially, a clear difference was seen between both groups. Also the stimulation-group achieved significantly higher reaction times than the control-group. But throughout the experiment, the reaction times in the stimulation group were strongly reduced while those of the control-group were slightly increased.

## 4. Discussion

To our knowledge this was the first study that investigated the effect of bi-hemispheric anodal tDCS over the primary motor cortex in MS patients, regarding motor control while performing a switching task so far. Despite the small number of subjects, we can cautiously say we found a positive result.

### 4.1. Rate of success (number of errors)

In general, the 3-limb and the heterolateral coordination condition were harder to perform regarding the numbers of errors. The homolateral coordination condition showed a significant reduction ( $p < 0.0001$ ). These effects were also found in previous research by Swinnen and Carson (2002). This study indicated that movements, requiring simultaneous activation of homologous muscles, were more accurately conducted than movements involving non-homologous muscles (Swinnen & Carson, 2002). This means that when subjects had to lift one hand and the ipsilateral foot, they made fewer mistakes. In addition to the heterolateral coordination condition, the three-limb coordination pattern was also more difficult to perform.

This is in line with earlier research from Meesen et al. (2006), indicating that coalition of constraints increases the degree of difficulty in motor coordination. The more difficult a combination, the more constraints had to be inhibited. For example, during a heterolateral combination more constraints had to be inhibited compared to a homolateral combination (Meesen, Wenderoth, Temprado, Summers, & Swinnen, 2006).

Since this study is the first bi-hemispheric tDCS study stimulating the M1 region, there are no equivalent studies performed. However, in the tDCS study by Leenus et al. in healthy participants, a significant reduction in number of errors was reported, but only for the heterolateral coordination condition. However, the stimulation site of this study was at the right dorsolateral prefrontal cortex (Leenus et al., 2015). Leite et al. (2011) performed a tDCS study (explained in the section 'Reaction Time'). No significant effects were found in the amount of errors made, when comparing the sites of stimulation and also when comparing the types of stimulation (Leite, Carvalho, Fregni, & Goncalves, 2011).

Also, the green switch cue resulted in fewer errors compared to the red switch cue ( $p = 0.0086$ ).

### 4.2. Reaction Time

Analogue with the rate of success, reaction time was best in the homolateral condition compared to the other conditions. This result can also be explained by the effect of coalition of constraints by Meesen et al. (Meesen et al., 2006).

Generally in switching tasks, reaction time increases and/or the number of errors decreases when the task switches. According to Schmitz & Voss (2014), task performance improves throughout the experiment, although the rate of improvement declines in every test block (Schmitz & Voss, 2014).

#### 4.3. Switch cost

There was a significant switch cost concerning the amount of errors. This means that, in general, trials that were preceded by a trial with a different pre-cue, were performed less accurately (explained in section Switch Cost). This was not the case for reaction time. For example, if a trial with a green pre-cue was preceded by a trial with also a green pre-cue, reaction time was significant better then when this trial would have been preceded by a trial with a red pre-cue.

Hsieh (2002) described the term switch cost as follows: 'Shifting task-set paradigm requires participants to alternate back and forth between two or more tasks. A robust finding is that, when a task is performed as a switch trial (Task B, then Task A), there is a sizable decrement in performance (in terms of either increased reaction time or decreased accuracy) compared to when it is performed repeatedly (Task A, then Task A). this decrement is called the shift cost' (Hsieh, 2002).

In our study, when performing the switching task, participants had to react to the green or the red pre-cue. Since the sequence was unpredictable, it was necessary to inhibit the motor paradigm of the previous trial and the participants had to prepare for the next trial. According to Meiran et al. (2000), the switching cost consists out of (at least) three components that reflect the passive dissipation of the previous task set, the preparation of the new task set, and a residual component (Meiran, Chorev, & Sapir, 2000). This 'passive dissipation' corresponds with the inhibition in our task.

This so called switch cost (shift cost) has been investigated in other studies. Leite et al. (2011) performed a tDCS experiment (over M1 or DLPFC) in which healthy participants performed a motor task and a cognitive task. For both tasks, they found smaller reaction times in the no shift condition compared with the shift condition. There was no difference concerning the type of stimulation (anodal, cathodal or sham), except for the cathodal stimulation that increased reaction times significantly compared to both sham and anodal stimulation. There were also no significant effects associated with the site of stimulation (Leite et al., 2011).

#### 4.4. tDCS versus sham

Some non-invasive brain stimulation studies have been performed to investigate motor control and coordination in MS patients, but mainly in healthy participants (Meesen et al., 2014). These studies make mostly use of motor tasks like a time reaction task, the go-no-go task or stop signal task. Primary outcomes are chiefly reaction time, accuracy or a combination of these two. So the main goal of these tasks is to perform them as quick as possible without making mistakes while receiving brain stimulation (J. W. Kwon et al., 2013; Lapenta, Fregni, Oberman, & Boggio, 2012; Leite et al., 2011; Stagg et al., 2011).

The most common areas to be stimulated are the (pre-) supplementary motor area, dorsolateral prefrontal cortex, right inferior frontal gyrus and the primary motor cortex. According to Hayduk et al (2013), anodal tDCS over the SMA has no effect on inhibition while performing a stop-signal reaction time task. This in contrast to the findings of Kwon et al. (2013), who concluded that atDCS over the SMA provides a reduction of the stop-signal reaction time and enhances the ability to inhibit certain

motor responses (Y. H. Kwon & Kwon, 2013). When applying atDCS over the pre-SMA, an improved inhibitory control was shown by Hsu et al. (2011) (Hsu et al., 2011). There was also a significant improvement seen while the right inferior frontal gyrus (rIFG) was activated (Jacobson, Javitt, & Lavidor, 2011). According to Meesen et al. (2013), atDCS over the primary motor cortex does not improve motor performance, which is contradictory to our results (Meesen et al., 2014).

However, this kind of inhibition refers to completely not executing a task (for example when hearing an auditory stimulus, the motor task should not be performed). The inhibition in our task is about inhibiting a motor strategy that was performed in the previous trial. Only one tDCS study was found to examine this sort of inhibition (Leite et al., 2011).

Our study reported a significant better reaction time in the stimulation group (for all combinations combined;  $p=0.0352$ ). There was no significant effect on the amount of errors made, although there was a tendency towards improvement ( $p= 0.0731$ ).

#### 4.5. VAS

No significant differences were found between the pre VAS scores of the intervention group and the control group (for all parameters), which means the groups were comparable at the start of the sessions. There was a significant difference between pre- and post-measurement in the stimulation group when looking at the parameter Fatigue, which indicates that the participants were less tired at the end of the session. This seems illogical, but the post-hoc power analysis revealed a very low power (17%), so this result should not be interpreted. This was also the case for the parameter Feeling Sickness, which meant participants should have felt worse afterwards (post-hoc power analysis was low: 27%). In the control group, there was a significant effect on attention in the post-VAS scores (post-hoc power analysis: 70%). This high power, although still lower than 80%, could be explained by the fluctuating symptoms in MS participants. When comparing post VAS scores of both groups, the parameter stress differed significantly ( $p = 0.0020$ ), but again, post-hoc power analysis revealed a low power (15%).

To check the mutual connection between two parameters, the correlation was measured between the VAS-scores of pre- and post-measurements of several parameters in both sessions. Values varying between (-)0.5 and (-)1 were considered a strong correlation (T. Vanhoornissen, 'Inductieve statistiek voor de gedragswetenschappen, toegepaste hypothesetoetsing met SPSS' (2012)).

In both pre- and post-measurements and in both sessions a strong correlation was found between sleep quality and attention, which seems logical. For the combinations between sleep quality and fatigue, as for the combination attention and fatigue, also a strong correlation was found. These rather unlogical correlations could again be due to the fluctuating symptoms of MS patients.

#### 4.6. Limitations and strengths of the study

Although our study shows some promising results concerning the application of tDCS in MS patients, some limitations should be taken into consideration. First, there was the relative small population.

Therefore we should be careful with generalizing the results. Second, the program only registered errors within the first 1000 milliseconds after displaying the stimulus. This means that if participants reacted slow (>1000 milliseconds) but reacted in a correct manner, this could not be extracted from our data. Even more, these 'blanco' results were interpreted as an error by the program. At last, the lack of experience of some researchers could also be one of the limitations, because this could have led to errors regarding the positioning of the electrodes, the program setting or saving the data.

The most important strength of the study according to us, is that it was the first bi-hemispheric (anodal) tDCS study that was performed in MS patients. This study aims to stimulate other investigators to do more research in this scarcely explored domain. Second, there was the development of a new motor task, the switching task. Because of the cognitive component it may be interesting for future studies investigating different neurodegenerative disorders (Alzheimer's Disease, Stroke, ...).

## **5. Conclusion**

The application of tDCS could be favorable during motor learning in MS patients, leading to improved reaction times and, lesser extent, to a reduction of errors. We recommend further research in this domain to confirm our results.





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Richting: **master in de revalidatiewetenschappen en de kinesitherapie-revalidatiewetenschappen en kinesitherapie bij musculoskeletale aandoeningen**

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