The effect of 10 Hz and 20 Hz transcranial alternating current stimulation on the synchronization of bimanual finger tapping.

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In accordance with the guidelines of the International Committee of Medical Journal Editors
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Acknowledgement

In this acknowledgement, the authors want to pay tribute to some people. First of all, we give a special thanks to Dr. Koen Cuypers, without his accompaniment and support this master thesis would not have been possible. Next we appreciate the Hasselt University and the REVAL center to give us the opportunity to complete this literature study and interesting research. Our thanks also go to everyone who has assisted us with advice. Finally, we also thank all the volunteers who participated in this study.

Sint-Truiden, 13 June 2016 L.VDB

Veerle, 13 June 2016 S.V.

Research context

This master thesis is written by two students of physiotherapy and rehabilitation sciences of the department medicine and life sciences UHasselt. The topic was provided by our promoter Dr. Koen Cuypers.

It is situated in the neurological branch of physiotherapy. The aim of this study is to explore the effects of transcranial Alternating Current Stimulation (tACS) on bimanual motor performance. The results of this study could be of great value to patients with neurological diseases. In this way, tACS might have a positive influence on the rehabilitation of motor coordination deficits.

During the first part of the master study, an overview of the existing literature about the effect of tACS on motor activity was given.

During this part of the master thesis, we focused on the effect of tACS on bimanual motor performance. The research that was conducted is described in the method part.

This master thesis is part of an ongoing project of Dr. Koen Cuypers. It is a pilot study for a larger project, namely 'the influence of transcranial alternating current stimulation (tACS) on motor control and motor performance.' It was carried out in the REVAL center of Hasselt University where all of the equipment is present.

Stefaan Vreys wrote the introduction and discussion, while Laura Van den Bergh wrote the research context, methodology and results parts. Both authors tested subjects, Laura Van den Bergh tested 17 subjects and Stefaan Vreys 13. Both authors immersed themselves in the statistical analysis to compare the results afterwards.

Abstract

Background

Different states of the brain, which have different functions in motor control, are related to different bands of rhythmic oscillating frequencies. It is hypothesized that transcranial alternating current stimulation (tACS) can entrain the rhythmic oscillations of the brain, and thereby influence motor control.

Objectives

The objective of this study was to investigate the effect of 10Hz and 20 Hz tACS on bimanual finger tapping in healthy adults.

Methods

30 subjects participated in the investigation and underwent two interventions (10 Hz, 20 Hz) and one placebo (low frequency transcranial random noise stimulation (LF tRNS)). Electrodes were applied on the motor cortex. A bimanual tapping task was performed in IN-phase and ANTI-phase. The purpose of the tapping task was to tap as synchronously as possible with both hands. The tapping synchronization between left and right hand was measured.

Results

Participants scored significantly better during IN-phase then during ANTI-phase tapping. Tapping synchronization was significantly better during 20Hz tACS compared to 10Hz tACS and the placebo (LF tRNS)

Conclusion

20 Hz tACS improves bimanual tapping synchronization compared to 10 Hz tACS and placebo (LF tRNS).

Introduction

Non-invasive brain stimulation is a way of inducing neuromodulatory effects on the cortex of the brain by using electromagnetic or electric current applied on the scalp. The most common techniques used for this stimulation are transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS). Because of the positive results of tDCS research, researchers have turned their attention to another way of transcranial electric stimulation, namely transcranial alternating current stimulation (tACS) (Zaghi, de Freitas Rezende, et al., 2010). Similar to tDCS, tACS is a non-invasive way of applying an electric current through the skull over the cortex of the brain. The difference between tACS and tDCS is the type of current used. tDCS uses direct current, which is a unidirectional flow of electric current, while tACS uses alternating current, which is a flow of electric current that periodically changes direction. The alternating current used in tACS has a sinusoidal waveform. In our research we will focus on tACS.

One of the possible underlying mechanisms that could explain the effects of tACS is the entrainment of neural oscillations (Zaghi, Acar, Hultgren, Boggio, & Fregni, 2010). The oscillatory activity can be measured on the scalp by electroencephalography (EEG). Research showed that different states of the brain are related to different bands of rhythmic oscillating frequencies. For example sleep is a low frequency band, and resting wake state is a high frequency band (Thut & Miniussi, 2009). Also for motor control there are bands of oscillation, which are linked to different functions (Wach et al., 2013a). For example alpha band oscillations (8-12Hz) are linked to automatic motor control (Pollok, Krause, Butz, & Schnitzler, 2009) while oscillations at the beta band (13-30 Hz) are linked to the control of more complex movements (Gerloff et al., 1998). This leads to the hypothesis that tACS can entrain the ongoing oscillations in the brain at the stimulating frequency (Zaghi, Acar, et al., 2010) (Zaehle, Rach, & Herrmann, 2010). We believe that by entraining these oscillations to a specific band, such as the alpha or the beta band, tACS can influence motor control.

A second possible underlying mechanism of tACS was suggested by Wach et al. (2013a)(Wach et al., 2013a). Wach et al. (2013a) found effects of tACS that could not be attributed to the entrainment of endogenous oscillations. Wach et al. (2013a) thinks these effects are the result of plastic alterations in the somatosensory cortex (S1) (Wach et al., 2013a). But there is no clear explanation on how these alterations occur.

An important difference between both mechanisms is that the entrainment effect occurs during stimulation (online effects), the plastic alterations in S1 will most likely occur after stimulation (offline effects). This means that it is possible that tACS induces effects which are the result of both underlying mechanisms.

The current knowledge on tACS is poor, which has several reasons. The most important reason is that the research on tACS is fairly new, so the number of studies on tACS is limited. Another reason is that the studies that where performed had a lot of variance between the stimulation parameters of tACS. For example duration of stimulation, frequency … This variance between parameters makes it difficult to compare the results of the different studies. The next reason is that the result of the studies had poor and conflicting evidence. This poor and conflicting evidence might be the result of the variation between the parameters. Finally not all underlying mechanisms of tACS are well understood, this makes it difficult to interpret results.

The goal of our study is to explore the effects of tACS on bimanual motor functioning in healthy young individuals. The goal of our research is to bring some new insights and contribute to the field of tACS research.

If tACS influences motor control, it might be of use in the rehabilitation of neuromuscular disorders. tACS might improve motor learning in rehabilitating patients, reduce bradykinesia and freezing in Parkinson patients, reduce chorea in Huntington patients, …

In this study we will compare the effects of 10 Hz tACS, 20 Hz tACS and sham stimulation on the synchronization of bimanual finger tapping. Our hypothesis is that 10 Hz tACS will improve motor function while 20 Hz tACS will slow down movement.

Method

Design

The study is a randomized controlled trial. All the participants will be subjected to three experimental conditions: two interventions (10 Hz and 20 Hz tACS) and one sham condition using low frequency transcranial random noise stimulation (LF tRNS). Participants, but not the investigators, were blinded towards the stimulation they received.

Medical ethics

The medical ethics committee of university hospitals KU Leuven has approved the protocol on the 25th august 2014. The application for adding an additional center in Hasselt was examined and approved on 5 December 2014 by the local ethics committee of the UHasselt. This made it possible to carry out the research in Hasselt as well. Prior to the study, participants filled out an informed consent.

Participants

There were 30 healthy subjects (14 male; 16 female) recruited for this study. The recruitment was done through oral communication and communication through social media. Inclusion and exclusion criteria were showed in table 1.

Table 1: Inclusion and exclusion criteria

Inclusion criteria	**Exclusion criteria**
• Right handed • Male or female between 18 and 30 years old.	• Left-handed • (Medical) condition that causes arm/hand function disorders • Metal in head • Pacemaker / Wires / Implantable Defibrillator • Metal artificial valve • Coronary artery bypass - clips • Biostimulator or TENS unit

	• Aneurysm clips (cerebral blood vessels, aorta, etc.)
	• Intracranial clips
	• Middle ear prosthesis (surgery of the ossicles)
	• Other prostheses or orthoses (if metal)
	• Implanted medication pump
	• Shrapnel (anywhere in the body)
	• Metalworker in the past
	• One of these had problems in the past:
	  ○ Cerebral Thrombosis
	  ○ Cerebral hemorrhage
	  ○ Head Trauma
	  ○ Meningitis
	  ○ Heart Attack
	  ○ Long period of unconsciousness (over 1 hour)
	  ○ Migraines
	  ○ Epilepsy
	• History of brain surgery
	• Family history of refractory epilepsy
	• History of active abuse of a substance during the last year
	• Possible pregnancy

Procedure

During this study tACS and tRNS was used. First, electrodes were placed on both sides of the head (for specific position, see appendix 1) one on the left and one on the right primary motor cortex. On the left side the electrode size were 25cm² (5 X 5 cm) and 50cm² (5 X 10 cm) on the right side. The task that the subjects completed was a tapping task and it consisted of 5 runs. In one run, lasting 4 minutes, they had to tap synchronically on the pace of an audio signal, with a fixed frequency of 1.5Hz. A run consists of 8 consecutive blocks. Each block is 30 seconds long. A block can have 4 different states (see table 2). In one run, each state is repeated twice. States were semi- randomized. More specifically, in the first 4 blocks state 1 to 4 were randomly assigned. This was repeated for block 5 to 8.

Table 2: Different states

State 1	IN-phase without stimulation
State 2	ANTI-phase without stimulation
State 3	IN-phase with stimulation
State 4	ANTI-phase with stimulation

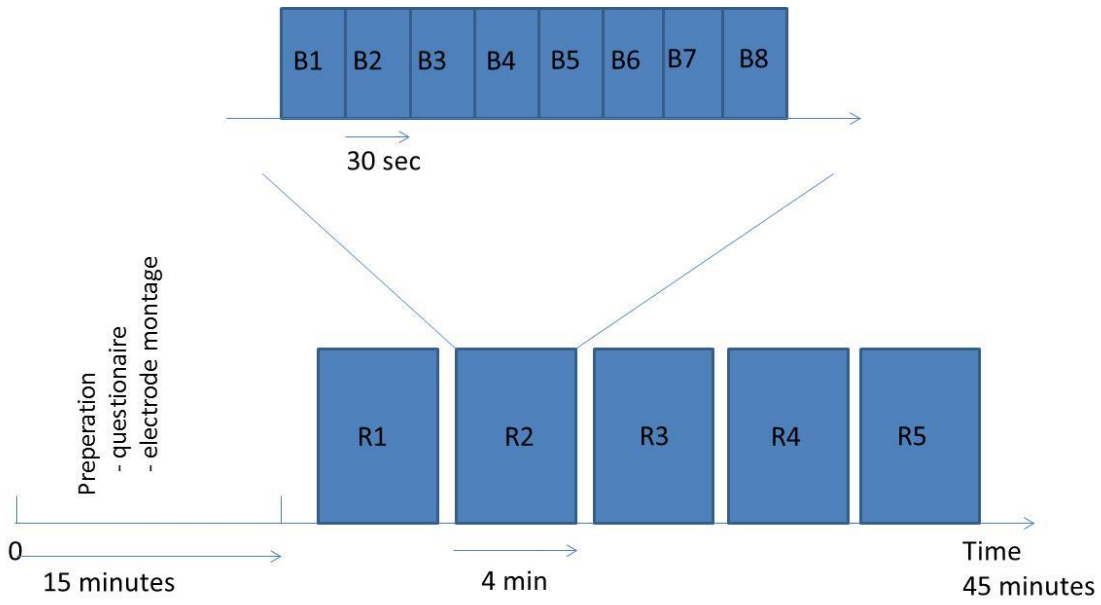


Figure 1: Overview method intervention; B= block; R= run

The middle and index finger of both hands were placed on sensors (buttons) to measure how simultaneous they tap, see figure 2. A metronome was used to set the rhythm.

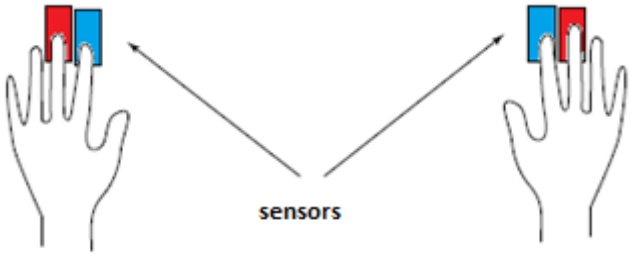


Figure 2: Placement hands.

IN-phase means that the participant has to tap alternating with both index and middle fingers on the sensors at the same time. In this case, the participant has to press either red sensors at the same time or both blue sensors. ANTI-phase means that the participant has to tap alternating with a different finger from both hands, using index and middle finger. In this case, the participant has to press one red and one blue sensor at the same time. Subjects can choose if they start using the index finger or the middle finger at the start of the block.

The randomization of the runs happened as follows: first, each state received a number. Next, the four numbers were written on a little piece of paper, every piece the same size. The pieces of paper were put in a box; it was shaken and thrown in the air. The piece of paper that landed the most on the left was the first state for that run, the second paper on the left was the second state and so on. This was done twice for each run. First run was randomized first and fifth run was randomized last.

During the task, the hands of the participants were covered by a piece of cardboard 30 cm above hands to prevent visual feedback. To have as few distractions as possible, the experiment was carried out in a small room with a white cloth covering all distractions.

Each participant was invited 3 times to our laboratory. They had to undergo the task with tACS twice (once at a stimulation frequency of 10 Hz and once 20 Hz) and one time with sham stimulation. Corresponding to the current knowledge LF tRNS was used for the sham condition. Terney et al. (2008) found that there are significant changes in motor evoked potentials (MEPs) using high frequency transcranial noise stimulation (HF tRNS), but found no significant changes in MEPs after LF tRNS (Terney, Chaieb, Moliadze, Antal, & Paulus, 2008).

The order of these 3 conditions was randomly chosen by the researcher when the participant arrived for the first time. Every intervention received a number (1: 10 Hz; 2: 20 HZ; 3: tRNS); these three numbers were put in a small box and thrown in the air. The number that landed most on the left became the first intervention and the number most on the right became the last and third intervention.

Before every intervention, the participants had to fill in a questionnaire about tiredness, alcohol and drug use, because these conditions can affect the results of the investigation.

Pilot study

First, a pilot study was performed. Four subjects participated in this study. The intervention happened the same way, but two keyboards were used and there was no control group. This pilot study was conducted to determine which keyboard to use for the real experiment. It was also conducted to master the standard procedure and make any potential changes. Every subject had to come back four times: 10 Hz tACS and keyboard 1; 10 Hz tACS and keyboard 2; 20 Hz tACS and keyboard 1; 20 Hz tACS and keyboard 2.

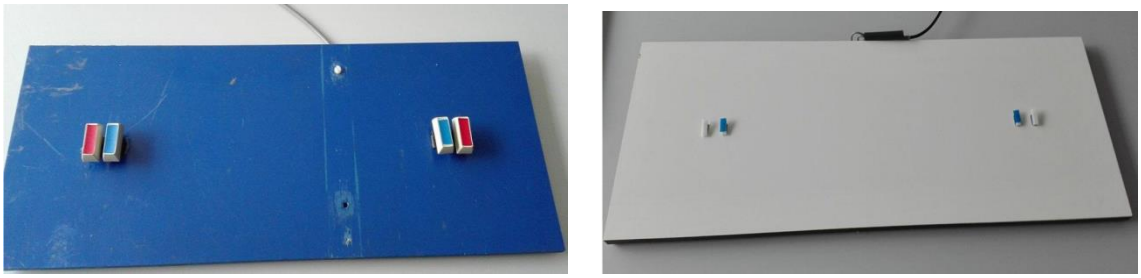


Figure 3: Different keyboards. Left: keyboard 1; right: keyboard 2.

After this pilot study, it was decided to use keyboard two. All subjects were allowed to choose the keyboard they preferred; all four preferred the second keyboard. Keyboard one often blocked, it would not cooperate and keyboard two was much more sensitive.
After this pilot study, it was also decided to use a control group, namely LF tRNS.

Outcomes

Primary outcomes

The primary outcomes are the tapping synchronization between both hands that will improve or deteriorate for 20 Hz and 10 Hz tACS.

Tapping synchronization is defined as the used finger on both hands is tapping the buttons simultaneously.

Secondary outcomes

There will be a questionnaire about tiredness because this may affect the primary outcomes.

Material and methods

While testing a DC stimulator was used for transcranial stimulation: tACS and tRNS. This stimulator is battery-driven (NeuroConn, Ilmenau, Germany) and the batteries are rechargeable.

The electrodes that were used in this study are conductive-rubber electrodes (NeuroConn, Ilmenau, Germany). They were put in a sponge and applied to the head with rubber bands. The sponges were soaked in NaCl 0.9%.

Taps were measured by the sensors on the tapping plate and processed at a sampling rate of 1000 Hz by an analog digital converter (Micro 1401 Cambridge Electronic Design, Cambridge, UK). The data were stored for offline analysis. Offline data processing and sorting was done using matlab (matworks, version 2013, beta). Using matlab, the tapping synchronization was measured [expressed as the total amount of time the required keys were pressed out of sync (further referred to as the term 'error'; an error reflects 1ms out of sync)]. An error means that at a 1ms interval on one hand side a button is pressed and not for the other hand side. Matlab calculated the total of errors for each state in each run. This means that there were 8 outcomes for each run.

Data analyses

The statistical analysis was performed using the JMP Pro 12 program. First, we checked whether the data were normally distributed, this on the basis of the Shapiro-Wilk test for each subgroup. 12 subgroups were made, namely 10 Hz tACS with the four different states; 20 Hz with the four different states and LF RNS with the four different states. This was done for the data with and without outliers. This test showed for each subgroup that the data were not normally distributed ($P < 0.05$). When the data was plot in a graph, a Gauss curve was seen. This curve should be transformed, but this transformation is too complicate. So normality will be assumed. Then the homogeneity of variance was checked by looking at the boxplots (figure 4 a till f). 3 subgroups were made, 10 Hz, 20 Hz and tRNS, this was done for data with and without outliers. For each intervention, the values of the different states were compared with each other. Because the box plots are about the same size, homogeneity can be assumed.

Finally, there was looked at the independence of the investigation. This is not a statistical test, but therefore was looked at the experimental design. The investigation has not met the criteria here, because there are repeated measures ANOVA.

Mixed models can only be used if independency is not achieved, but the normality and homogeneity do. For this study, these assumptions are not achieved. Due to our limited knowledge of statistics, mixed models will be used in this master thesis despite failure to meet assumptions. This decision was in consultation with statisticians Mrs Prenen and Mrs Nysen. Phase, stimulation and frequency are the fixed effect, the Y = data and the random effect are the subjects. The differences shall be taken into account at baseline between subjects.

The data will be analyzed, and there will be a comparison between the model with outliers, and the model without the outliers. An outlier is defined as a value deviating more than 2 standard deviations and also when the subject tapped incorrect during the first 4 seconds. The latter was checked manually. The standard deviation was calculated separately for each subject and for each intervention. 31 values were excluded.

Results

All participants have successfully completed the study. At the end of the experiment, the subjects received the three different interventions, namely 10 Hz tACS, 20 Hz tACS and LF RNS.

In the results, there is a comparison between the data with and without outliers.

Homogeneity of Variance

To determine the homogeneity of variance, there was looked at the box plots. 3 subgroups were made: 10 Hz, 20 Hz and tRNS. This was done for data with and without outliers. Because the box plots are about the same size, homogeneity can be assumed.

In figure 4d, 4e and 4f the outliers were removed (defined in method), but there are still some outliers visible in accordance with this statistical analysis. These are the values in which the subjects started well, but made a mistake during the run after four seconds or tapped asynchronously.

With outliers

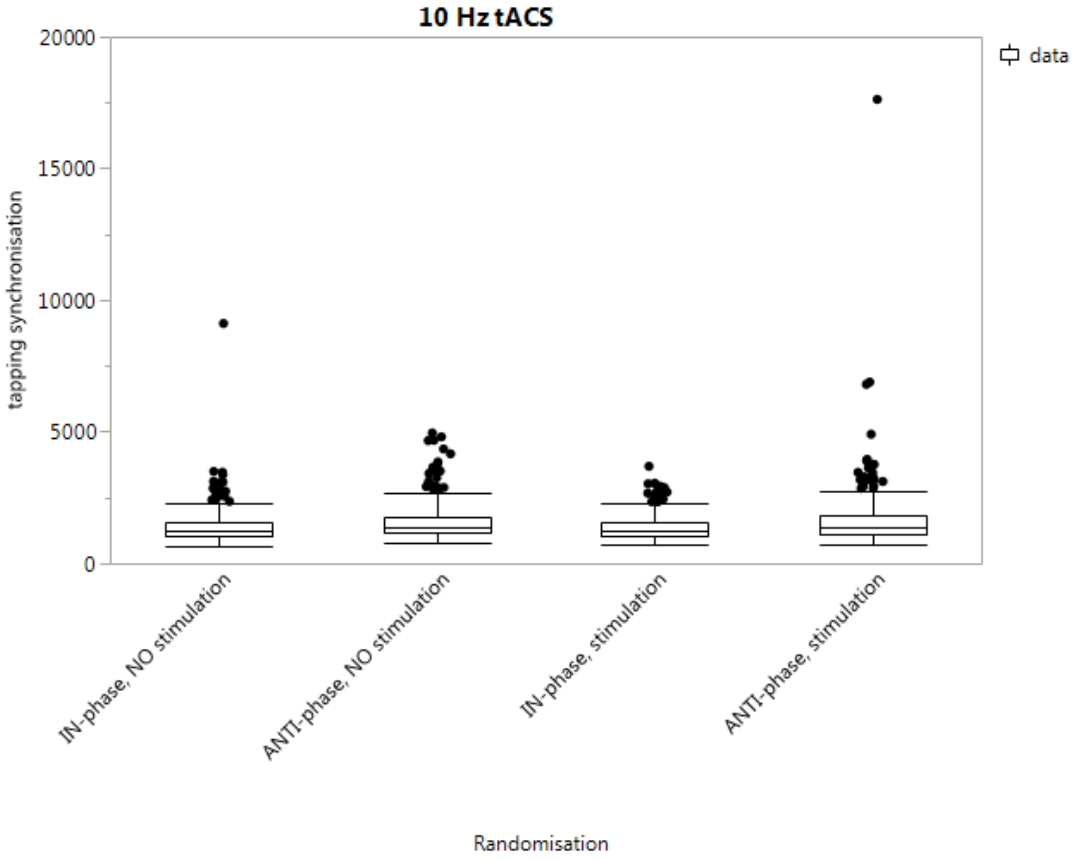


Figure 4a: Synchronization variability for 10 Hz frequency. Data plotted as group mean ± standard deviation (SD). Model with outliers.

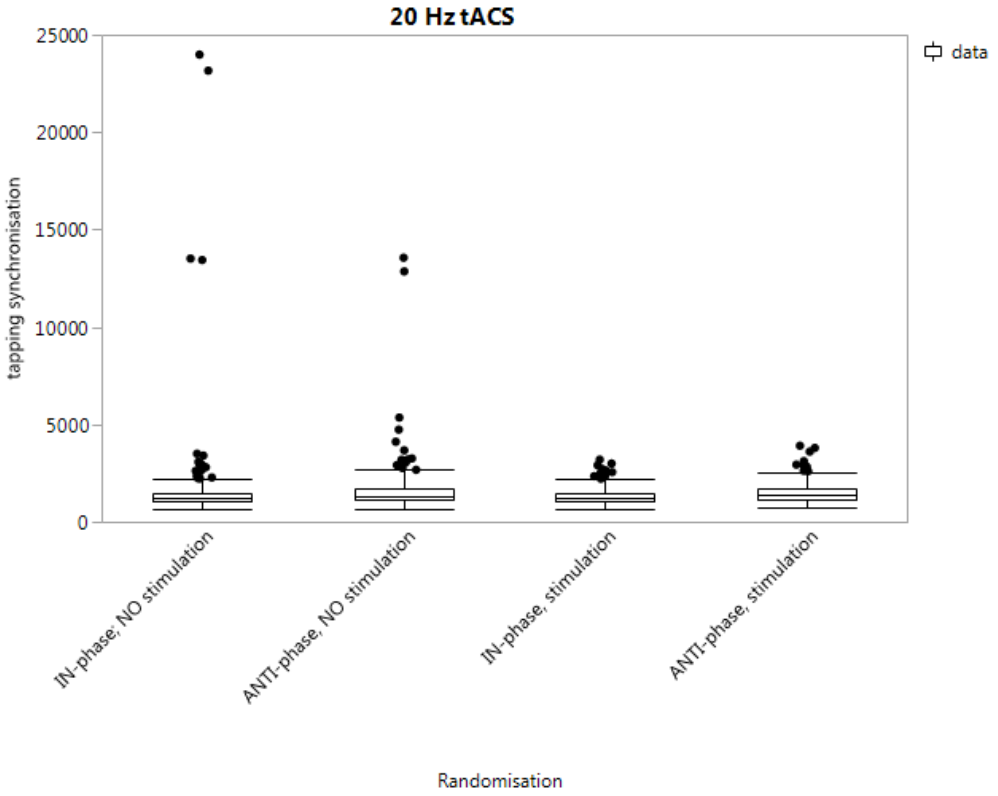


Figure 4b: Synchronization variability for 20 Hz frequency. Data plotted as group mean ± standard deviation (SD). Model with outliers.

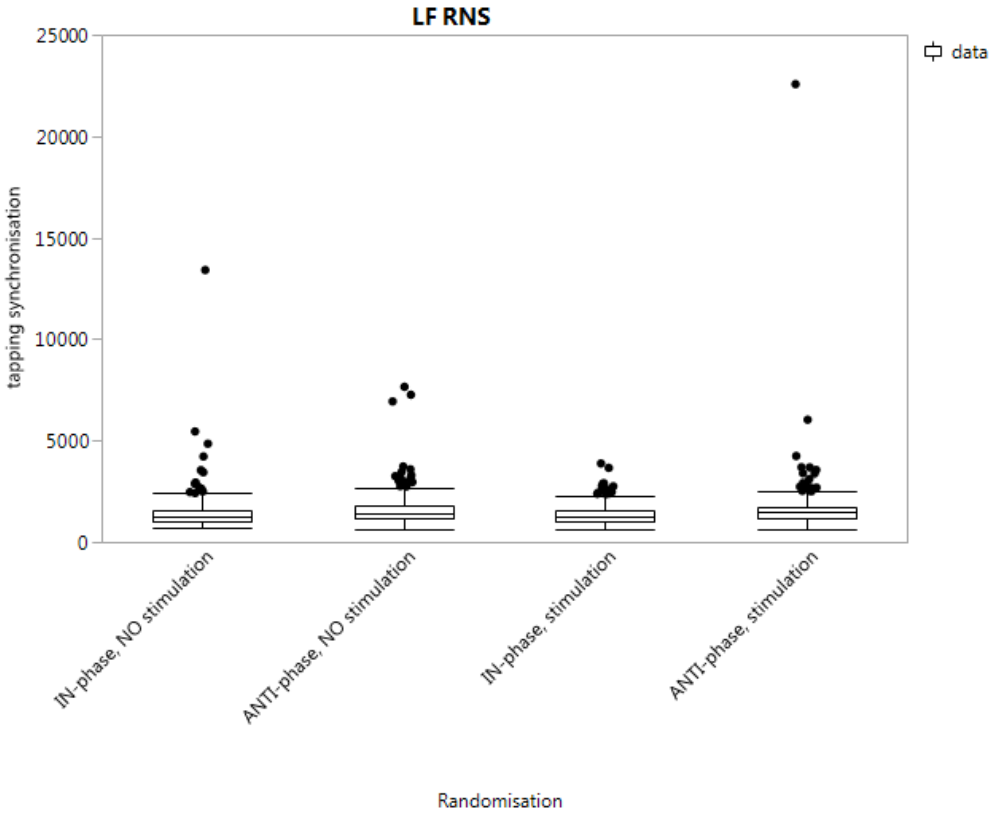


Figure 4c: Synchronization variability for tRNS frequency. Data plotted as group mean ± standard deviation (SD). Model with outliers.

Without outliers

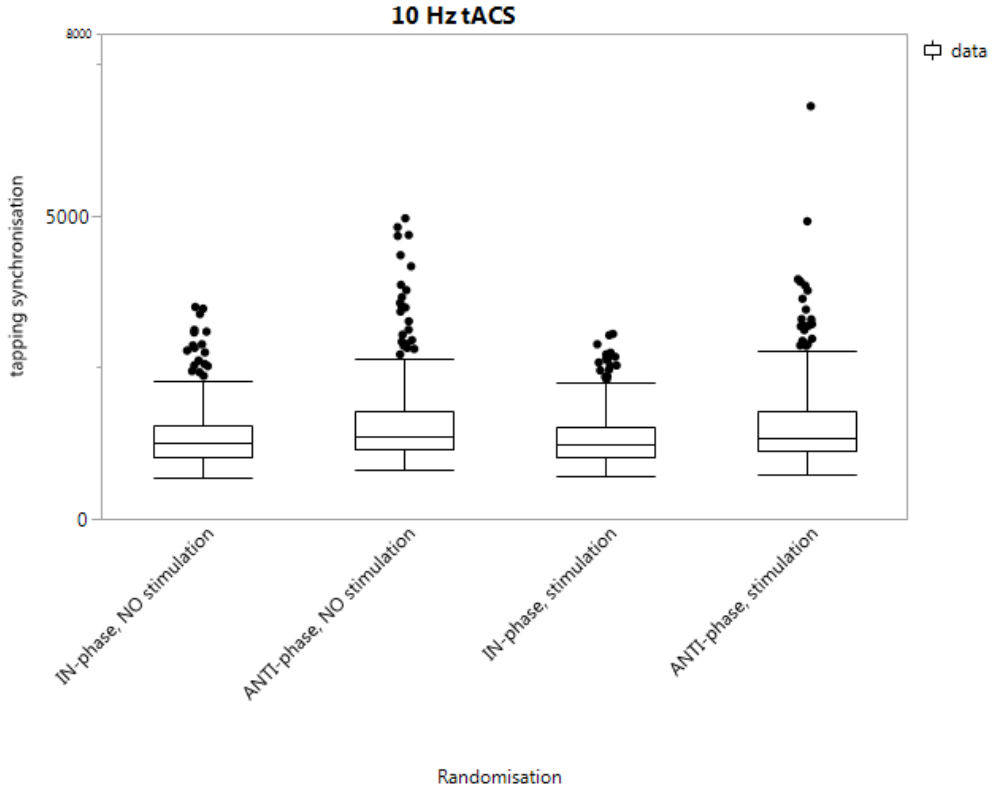


Figure 4d: Synchronization variability for 10 Hz frequency. Data plotted as group mean ± standard deviation (SD). Model without outliers.

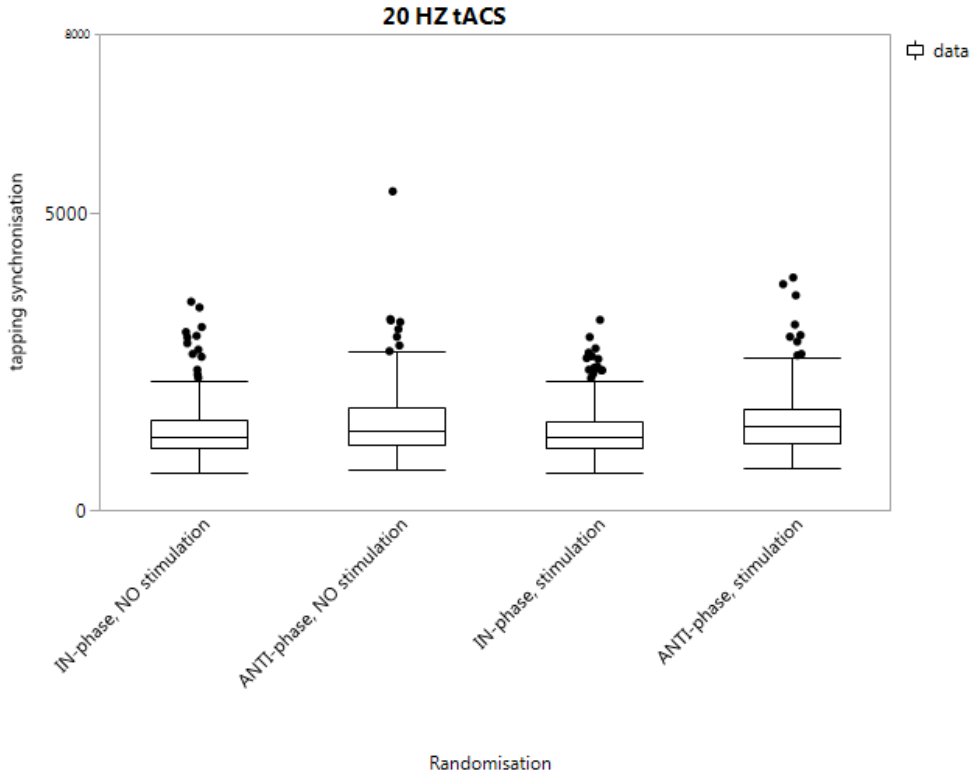


Figure 4e: Synchronization variability for 20 Hz frequency. Data plotted as group mean ± standard deviation (SD). Model without outliers.

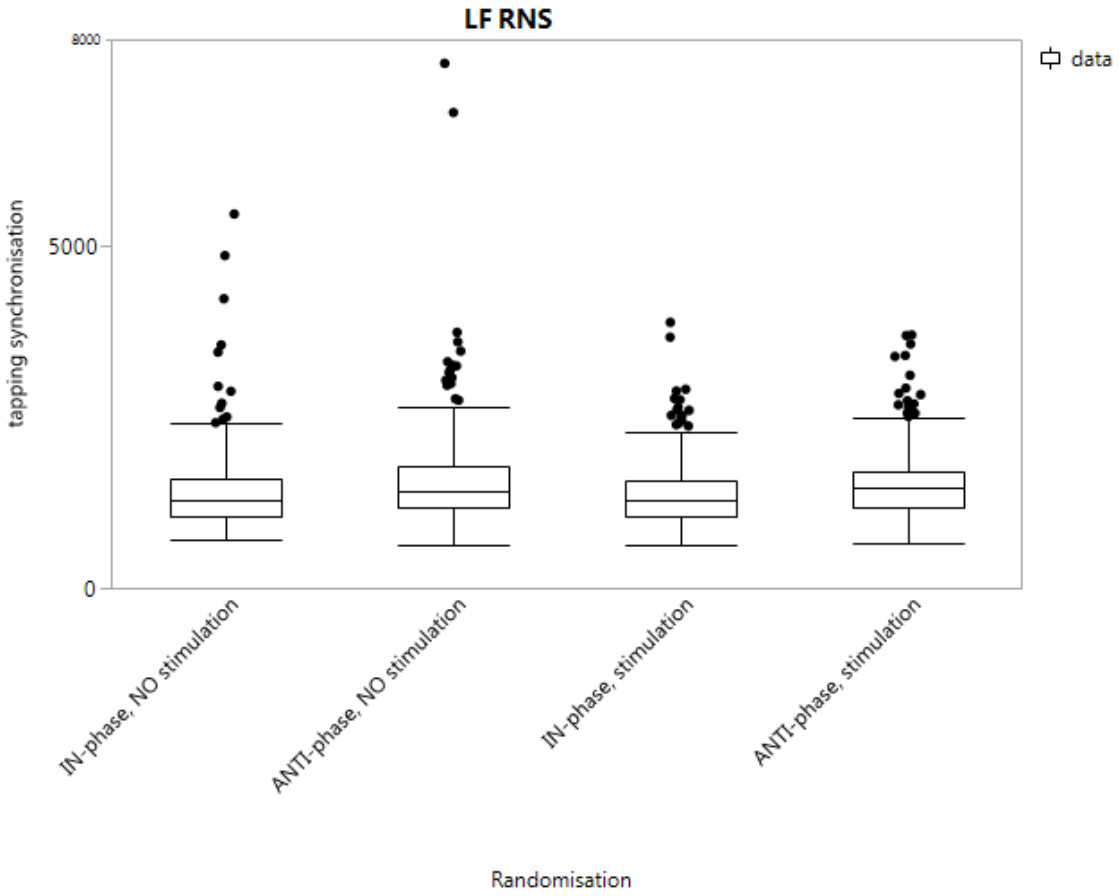


Figure 4f: Synchronization variability for TRNS frequency. Data plotted as group mean ± standard deviation (SD). Model without outliers.

General comparison between the conditions

Data are shown for the three different frequencies and further split for phase and stimulation (figure 5 and 6).

With outliers

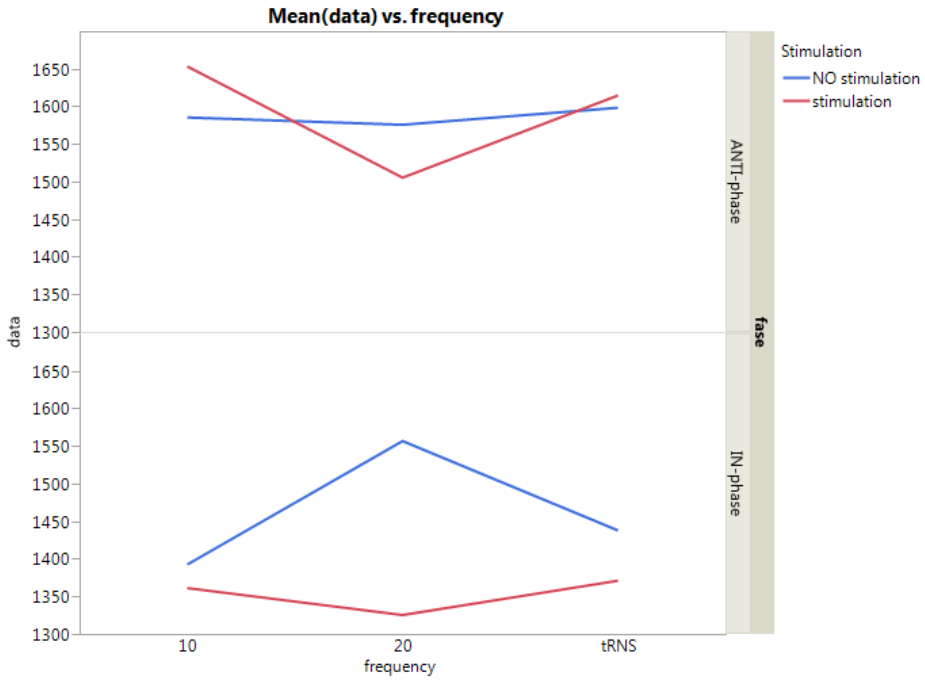


Figure 5: Synchronization variability for the three different frequencies and further split for phase and stimulation. Data plotted as group mean. Model with outliers.

Without outliers

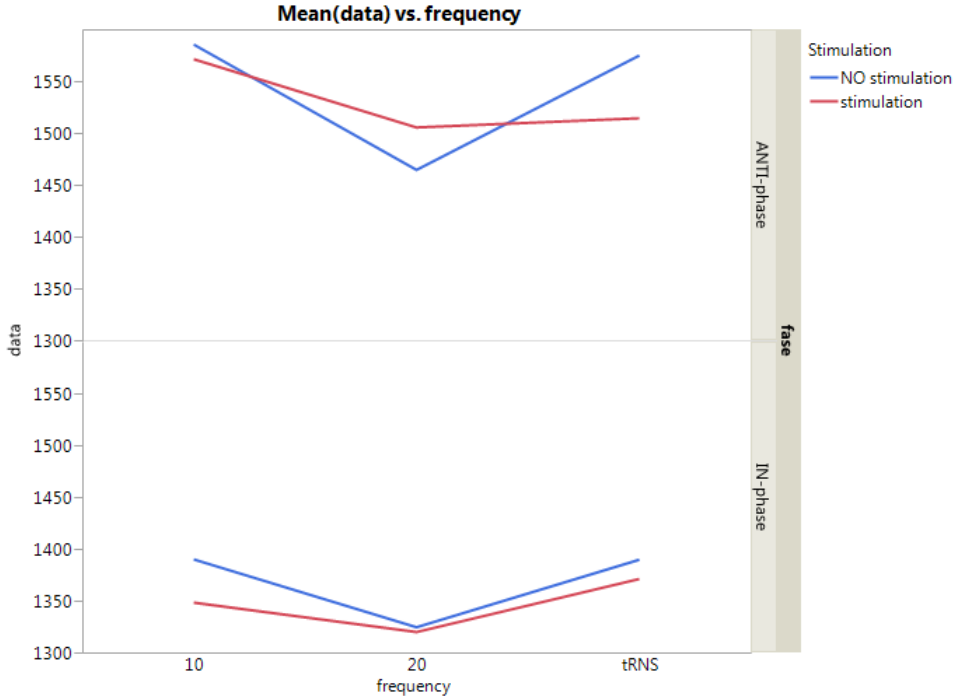


Figure 6: Synchronization variability for the three different frequencies and further split for phase and stimulation. Data plotted as group mean. Model without outliers.

Comparison between the conditions and interactions

Once the full model is fit, the non-significant interactions can be deleted one by one, starting with the interactions with the largest p-value and subsequently fitting the model.

With outliers

Table 3a: Fixed effect tests

	P Value
frequency	0.9308
fase	< 0.0001
Stimulation	0.0803
frequency*fase	0.1344
frequency*Stimulation	0.0582
fase*Stimulation	0.0573
frequency*fase*Stimulation	0.8487

Table 3a: mixed models; full factorial. Model with outliers. Significant changes are indicated.

Table 3b: Fixed effect tests

	P Value
frequency	0.9309
fase	< 0.0001
Stimulation	0.0806

Table 3b: mixed models; the non-significant interactions were deleted one by one, starting with the interactions with the largest p-value. Model with outliers. Significant changes are indicated.

Including the outliers, there was observed a significant value only for phase ($p < 0.05$) (table 1a and 1b). This means there is a difference between IN-phase and ANTI-phase.

Without outliers

Table 4a: Fixed effect tests

	P Value
frequency	< .0001
fase	< .0001
Stimulation	0.2295
frequency*fase	0,2009
frequency*Stimulation	0.2885
fase*Stimulation	0.5402
frequency*fase*Stimulation	0.3230

Table 4a: mixed models; full factorial. Model without outliers. Significant changes are indicated.

Table 4b: Fixed effect tests

	P Value
frequency	< 0.0001
fase	< 0.0001
Stimulation	0.2289

Table 4b: mixed models; the non-significant interactions were deleted one by one, starting with the interactions with the largest p-value. Model without outliers. Significant changes are indicated.

When the outliers were obtained from the data, there were significant values observed for phase and frequency ($p<0.05$) (table 4a and 4b). For phase, this means there is a difference between IN-phase and ANTI-phase. The Tukey HSD (table 5) showed that there were significant differences between 10 and 20 Hz and between 20 Hz and TRNS.

Table 5: Multiple comparison (Tukey HSD).

Frequency	Prob> |t|
10 Hz vs 20 Hz	0.0002
10 Hz vs tRNS	0.7647
20 Hz vs tRNS	0.0023

Table 5: Difference between interventions. Data without outliers.

Sensitivity of the stimulation

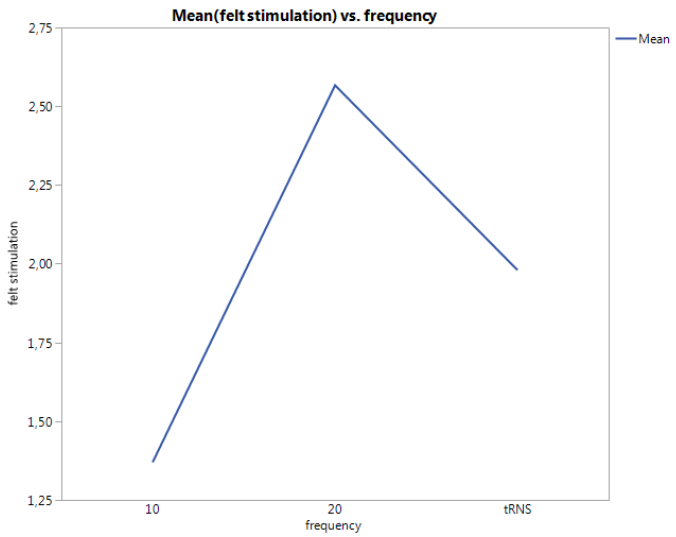


Figure 7: Stimulation felt by frequency on a scale of 0 -10

After each intervention the subjects were asked about the intensity of the stimulation which they had to indicate on the basis of a VAS-scale of 0 to 10. In Figure 7 can be seen that the perceived intensity of stimulation was the highest at the intervention with 20 Hz tACS, but these differences are not significant (p value = 0.1037). A mixed model was used with frequency as fixed effect and subjects as random effects.

Questionnaires

For each intervention, the participants filled in a questionnaire about tiredness, alcohol and drugs. Only the first time there was a questionnaire about right-handedness and whether they played a musical instrument or not.

Musical instruments

There was looked if some of the participants played the piano, because they may have more experience with tapping. None of the participants played the piano.

Right-handedness

Five out of 30 subjects were not perfect right-handed with a score of 10 +. The scores range from 5+ till 9+. No statistical analysis was performed. There was looked at differences in averages for each intervention and the number of outliers. There were no notable differences with other subjects visible.

Tiredness

No statistical analysis was performed. There was checked individually for each subject for differences between the fatigues of interventions. If there was a difference of five or more, the averages for each intervention were observed and the number of outliers. Four out of 30 subjects had a difference of tiredness. Three of these subjects made the most mistakes when they were the most tired.

Alcohol

No statistical analysis was performed. When a subject consumed more than 12 alcoholic drinks the night before, there was looked at differences in averages for each intervention and the number of outliers. Five out of 30 subjects consumed at least one time more than 12 alcoholic drinks. Two of these subjects scored worse the day after drinking.

Drugs

There was not asked which type of drug the participants used. No statistical analysis was performed. There was looked at differences in averages for each intervention and the number of outliers if the subject used drugs the day before intervention. Only one subject used drugs the day before and no differences were visible.

Discussion

The results of the study show that the synchronization of bimanual finger tapping during IN-phase is better than during ANTI-phase. This is what we expected and what is already been shown in other studies. ANTI-phase is more variable for the same movement frequency then IN-phase (Kelso, 1984) (Schoner, Haken, & Kelso, 1986).

After removing the outliers, the most important finding of this study is that 20 Hz tACS improved synchronization of bimanual finger tapping. So we can conclude that there is obviously an influence of 20 Hz tACS on the synchronization. But there is no significant interaction between frequency and stimulation. So there is no difference in results between the states with stimulation compared to the states without stimulation. This means that the effect of tACS must be carried over from a state with stimulation to a state without stimulation. This leads to the conclusion that 20 Hz tACS has both online and offline effects. The online effects of tACS can be attributed to the entrainment of endogenous oscillations. (Helfrich et al., 2014; Zaehle et al., 2010; Zaghi, de Freitas Rezende, et al., 2010) But according to Vossen et al. (2015) entrainment of endogenous oscillations is not strong enough to outlast stimulation. (Vossen, Gross, & Thut, 2015) Vossen et al. (2015) and Zaehle et al. (2010) suggest that plasticity mechanisms are the underlying mechanism for the aftereffects of tACS. (Vossen et al., 2015; Zaehle et al., 2010) These plasticity mechanisms are spike-timing-dependent plasticity (STDP). Vossen et al. (2015) found that blocks of 10 seconds of 10Hz tACS resulted in significant after effects. (Vossen et al., 2015) These after effects were the result of STDP, but blocks of 3 seconds of 10Hz tACS had no significant after effects. As the blocks in our study are 30 seconds it is plausible to say that the after effects are also the result of STDP. So the STDP is a possible explanation for the after effects of tACS in this study.

In a previous literature study we concluded that 10 Hz tACS will improve motor function and 20 Hz tACS will slow movement. From these findings a hypothesis was formed that 10 Hz tACS would improve the bimanual tapping synchronization while 20 Hz tACS would deteriorate the bimanual tapping synchronization. The results of the current study are not in line with that hypothesis. Because the studies that were included in the literature study

involved unimanual tasks, the results of the literature study might not be applicable to the current study. The brain interactions during bimanual tasks are different than during unimanual tasks. In unimanual tasks the contralateral hemisphere of the brain is responsible for the movement. (Chen, Gerloff, Hallett, & Cohen, 1997; Kim et al., 1993; Kristeva, Cheyne, & Deecke, 1991) In bimanual movements both hemispheres are active, but above all the dominant hemisphere. (Jancke et al., 1998; Serrien, Cassidy, & Brown, 2003; Viviani, Perani, Grassi, Bettinardi, & Fazio, 1998) During bimanual tasks there is an increased coupling between left and right sensorimotor cortices which mostly consists of a drive from the dominant to the non-dominant hemisphere. (Serrien et al., 2003) Serrien et al. (2003) also found that this drive from the dominant to the non-dominant hemisphere was in the Beta band range and increased during activity compared to rest state. In this study Serrien et al. (2003) also found that when the bimanual movement was brought out of balance by loading one side, this decreased the drive in the Beta band and also decreased the behavioral results. (Serrien et al., 2003) In another study Serrien et al. (2002) found that increasing the speed of a bimanual task decreased the interhemispheric coupling in the Beta band. (Serrien & Brown, 2002) As a result of the decreased interhemispheric coupling in the Beta band the behavioral performance also decreased. Consequently, it can be concluded that the interhemispheric coupling in the Beta range is important in bimanual movements. It could be possible that by improving this coupling you might improve the behavioral performance of bimanual movement. This is also in line with the results of our study where 20 Hz tACS improved the synchronization of bimanual movement. The results from Serrien et al. (2003, 2002) and from our study are not strong enough to make any conclusions about this theory, but there are strong indications that further research can lead to positive results.

Prior to our study we hypothesized that tACS might have a stronger influence on more difficult tasks. (Sadato, Yonekura, Waki, Yamada, & Ishii, 1997; Swinnen et al., 1998) So we included ANTI-phase and IN-phase in our study to compare the influence of tACS in both phases. However, while there was a significant effect from 20 Hz tACS, the effect of tACS was the same for both phases. Certainly in our study the effect of tACS was not more pronounced with more complex tasks.

Strengths of the study:

Prior to the study the researchers did a pilot study. So the researchers could become familiar with the testing protocol and train the practical aspect of the protocol as are for example the application of the electrodes. The pilot study also made the researchers able to test two different keyboards and select the best. The pilot study helped to improve the testing protocol.
In this study there was a standardized testing protocol that was the same for all the participants.

Limitations and weaknesses of the study:
The blinding of the study was not optimal. The researchers were not blinded. But because the investigators did not do any of the measuring, the influence of the non-blinded investigators on the results is limited. A more important problem was that some of the subjects were aware of the stimulation. They could feel the difference between a state with stimulation or without stimulation. This might have had an influence on the results. The maximum influence occurred at the stimulation with 20 Hz tACS.
Another limitation is the statistical analysis. The analysis of this data is complex. Because this is a master thesis and we have limited experience in statistical analysis of such complex data, we decided to choose the most viable way to analyze the data.

Possible errors of study:
A possible error in the study is that the impedance of the tACS during stimulation is not taken into account. Before starting every session the researchers made sure the impedance was below 50 kΩ. This because the stimulator would stop stimulating due to safety reasons at impedance levels higher than 50 kΩ. It is possible that the effects of tACS would have been larger if the impedance was kept below 5kΩ as in the studies of Wach et al. (2013a, 2013b) and Antal et al. (2008), or below 10 kΩ as in the study of Fuerra et al. (2011). (Antal et al., 2008; Feurra et al., 2011; Wach et al., 2013a, 2013b)
Very probably tiredness had a negative influence on the results, but we have no statistical data to prove this hypothesis
There is no good placebo for tACS; the only way to induce the feeling of tACS is by using tACS. So if you want a placebo that gives the feeling of tACS you need to use a form of tACS that has no effect. Based on one study of Terney et al. (2008), who found that there are

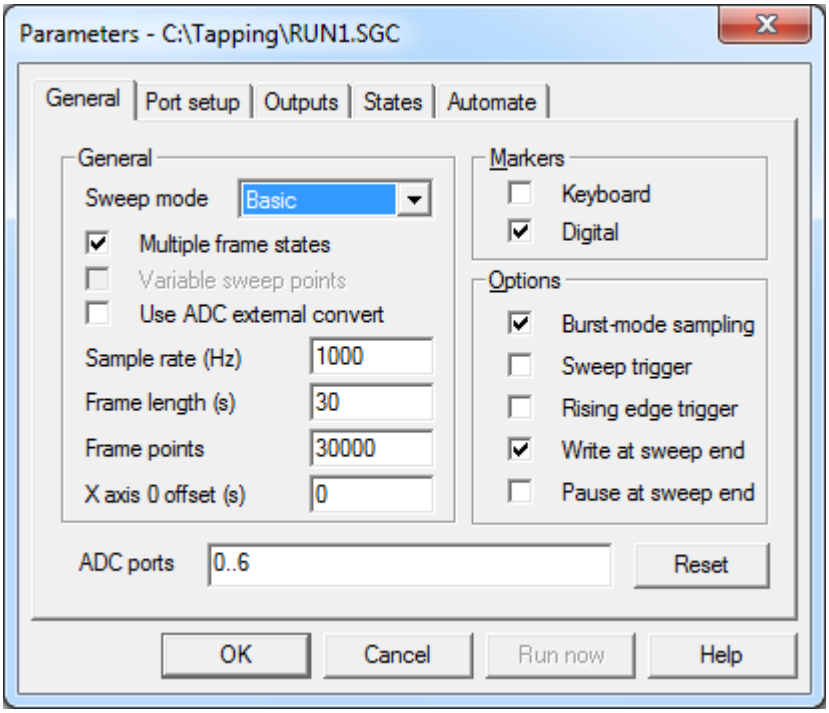
significant changes in MEPs using HF tRNS, but no significant changes in MEPs after LF tRNS (Terney et al., 2008), we opted for LF tRNS as a placebo. However, this choice was based on only one study and it might be possible that LF tRNS has yet an effect, not detected by Terney et al. (2008).

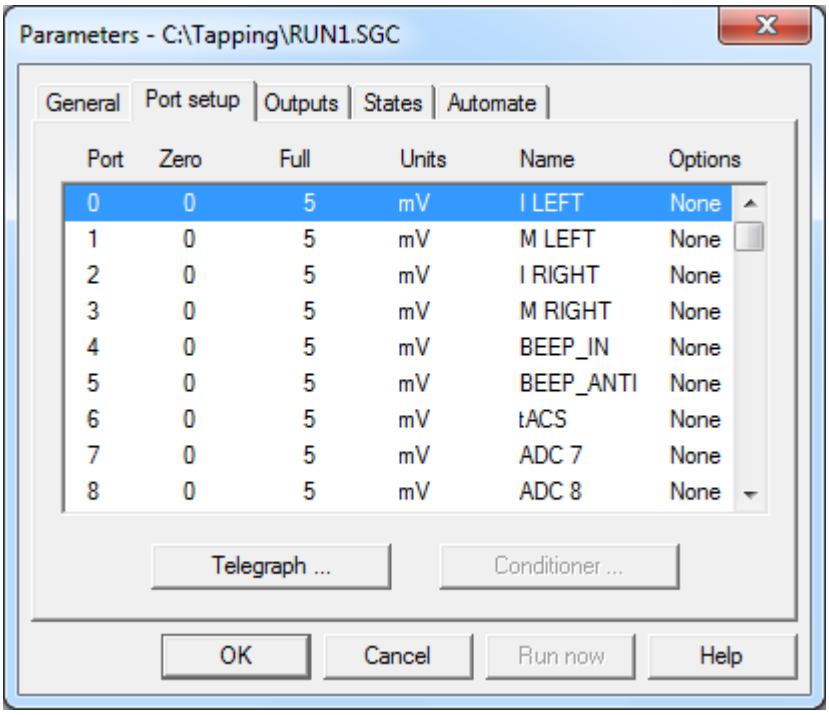
Appendix

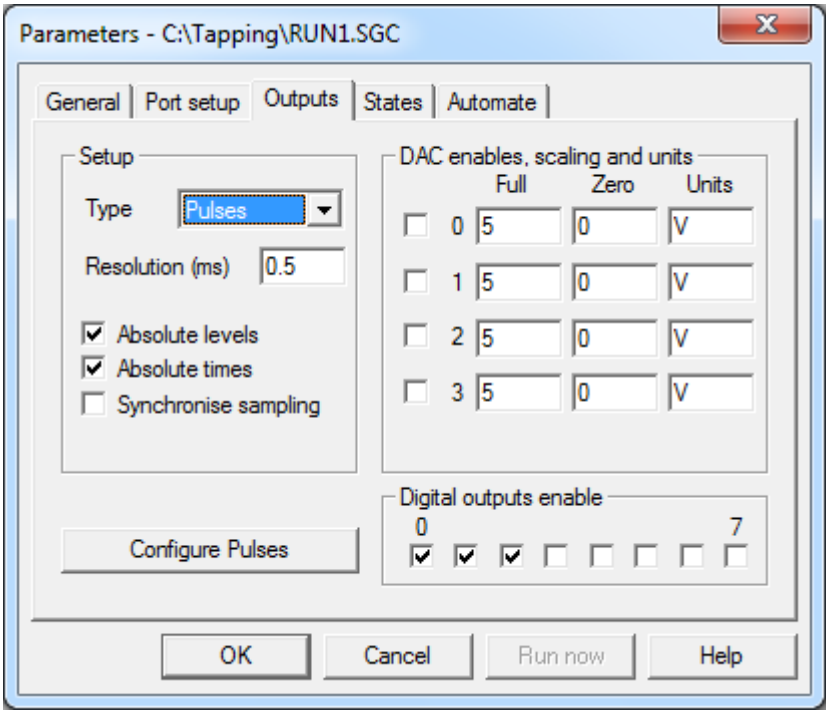
Appendix 1: Draaiboek

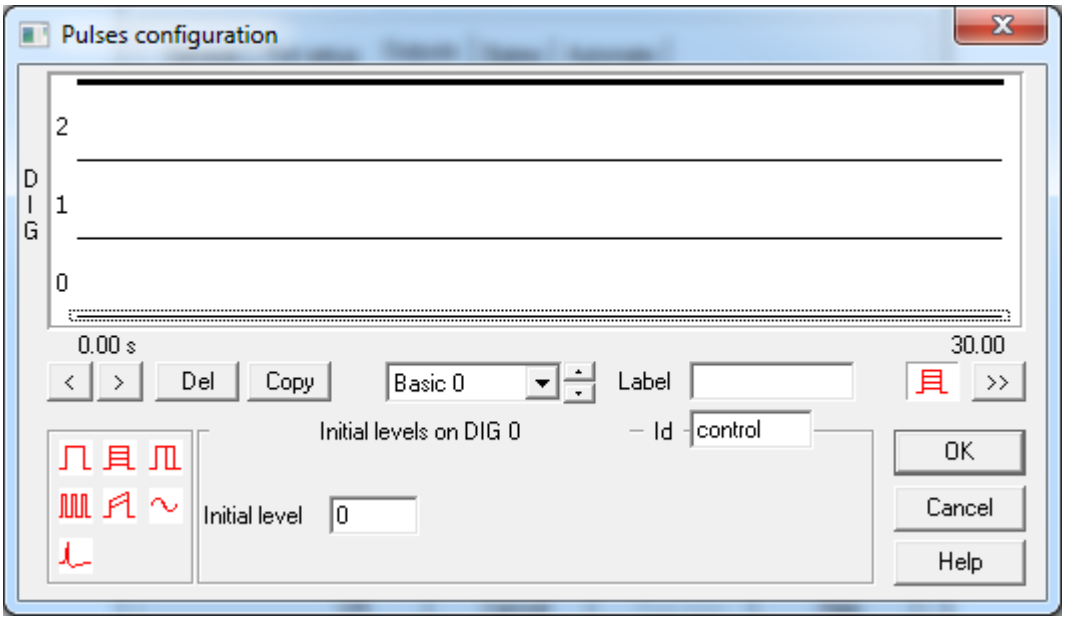
Instellingen protocol computer

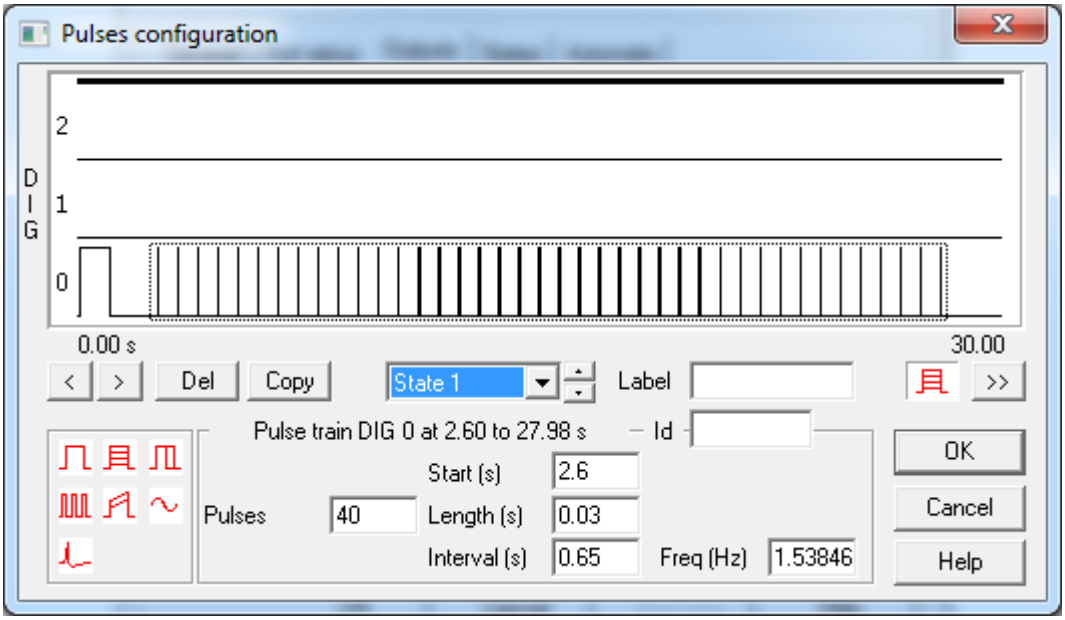
RUN 1

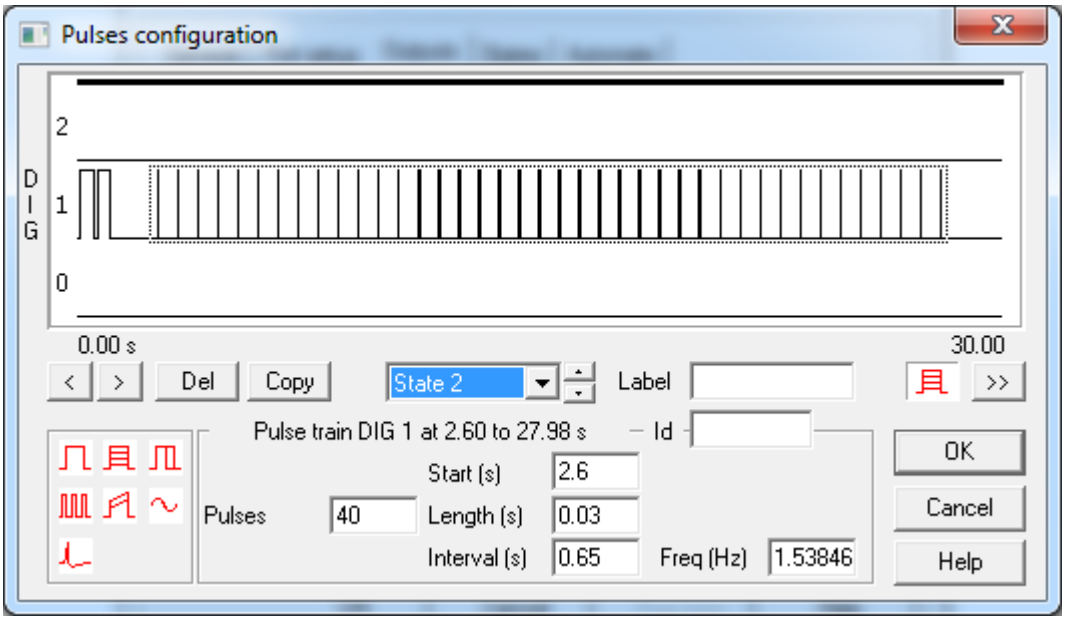


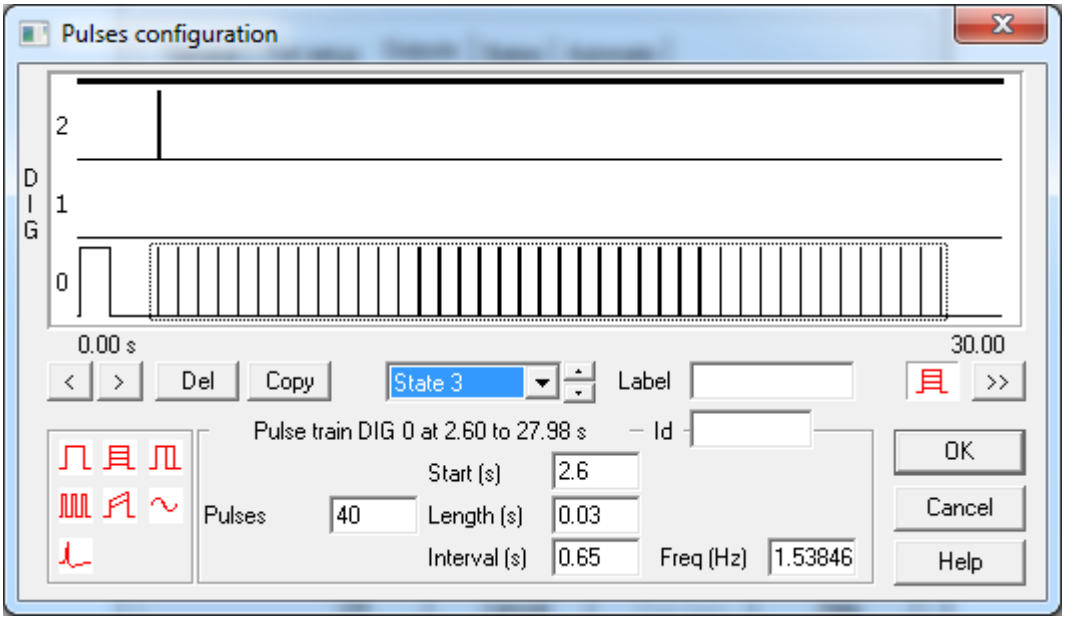


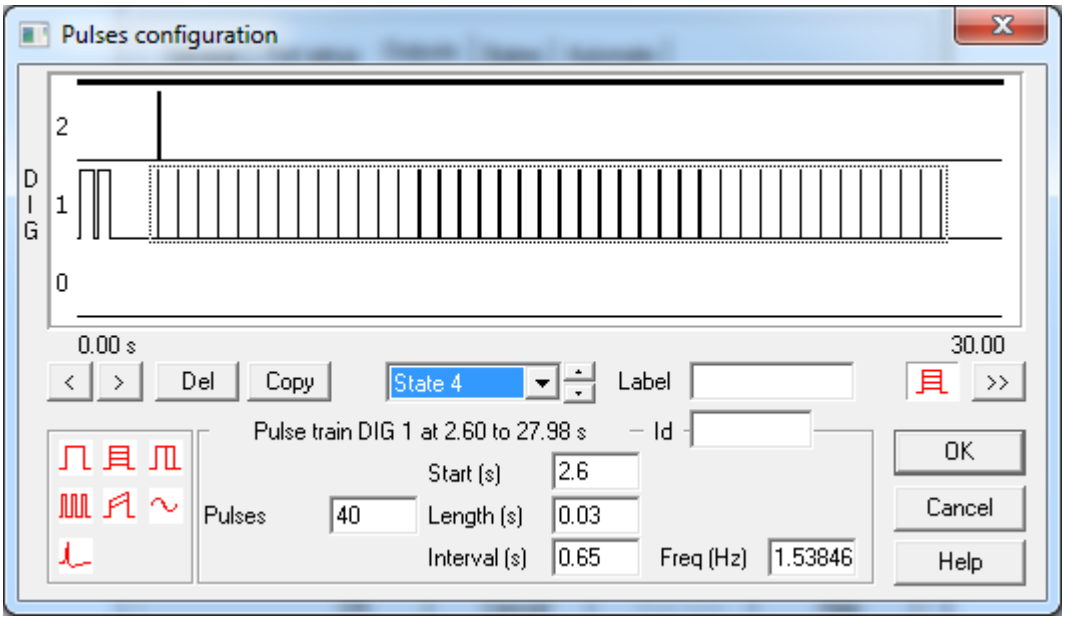

Parameters - C:\Tapping\RUN1.SGC
General
Port setup
Outputs
States
Automate
Setup
Type
Pulses
Resolution (ms)
0.5
Absolute levels
Absolute times
Synchronise sampling
DAC enables, scaling and units
Full
Zero
Units
0 5 0 V
1 5 0 V
2 5 0 V
3 5 0 V
Digital outputs enable
0
7
Configure Pulses
OK
Cancel
Run now
Help

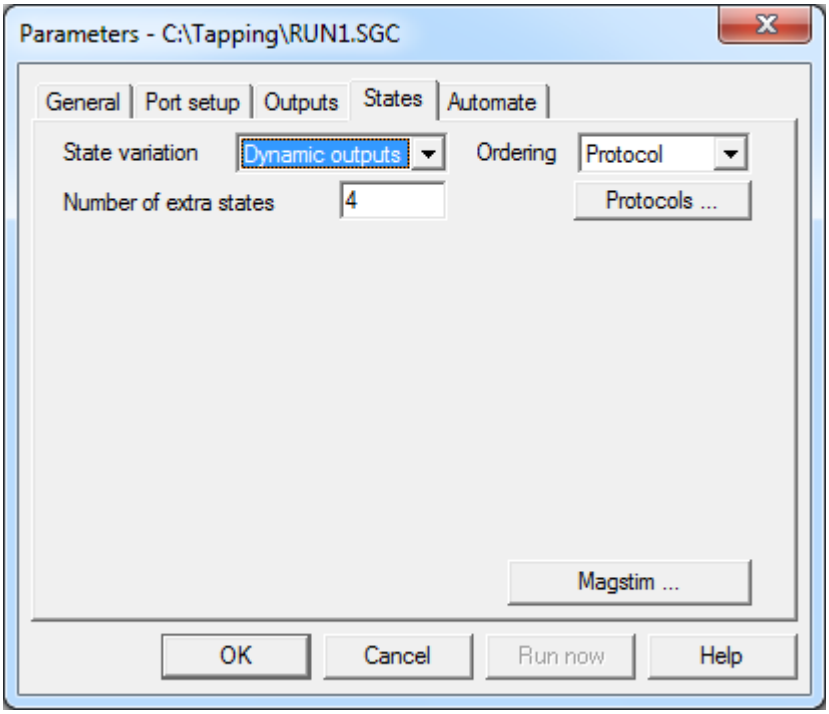

Pulses configuration
DIG
2
1
0
0.00 s
30.00
Del
Copy
Basic 0
Label
>>
Initial levels on DIG 0
Id
control
Initial level
0
OK
Cancel
Help

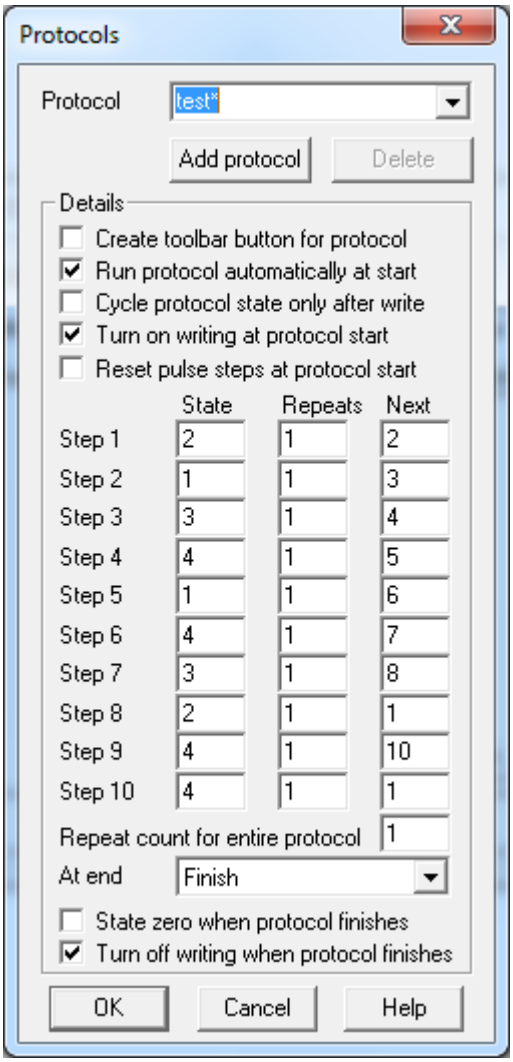

Pulses configuration
DIG
2
1
0
0.00 s
30.00
Del
Copy
State 1
Label
>>
Pulse train DIG 0 at 2.60 to 27.98 s
Id
Start (s)
2.6
Pulses
40
Length (s)
0.03
Interval (s)
0.65
Freq (Hz)
1.53846
OK
Cancel
Help

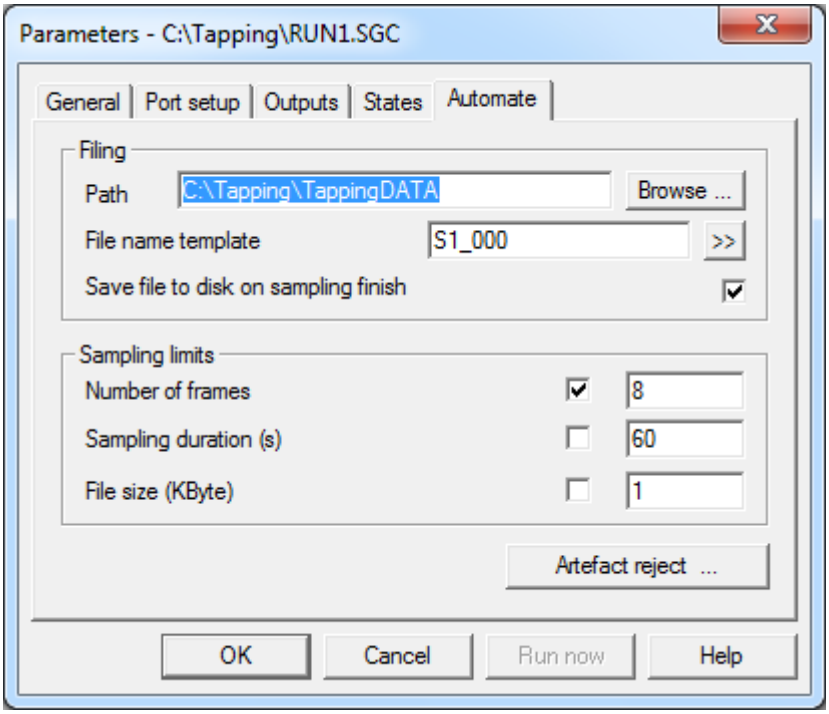

Pulses configuration
DIG
2
1
0
0.00 s
30.00
Del
Copy
State 2
Label
>>
Pulse train DIG 1 at 2.60 to 27.98 s
Id
Start (s)
2.6
Pulses
40
Length (s)
0.03
Interval (s)
0.65
Freq (Hz)
1.53846
OK
Cancel
Help


Pulses configuration
DIG
2
1
0
0.00 s
30.00
Del
Copy
State 3
Label
>>
Pulse train DIG 0 at 2.60 to 27.98 s
Id
Start (s)
2.6
Pulses
40
Length (s)
0.03
Interval (s)
0.65
Freq (Hz)
1.53846
OK
Cancel
Help

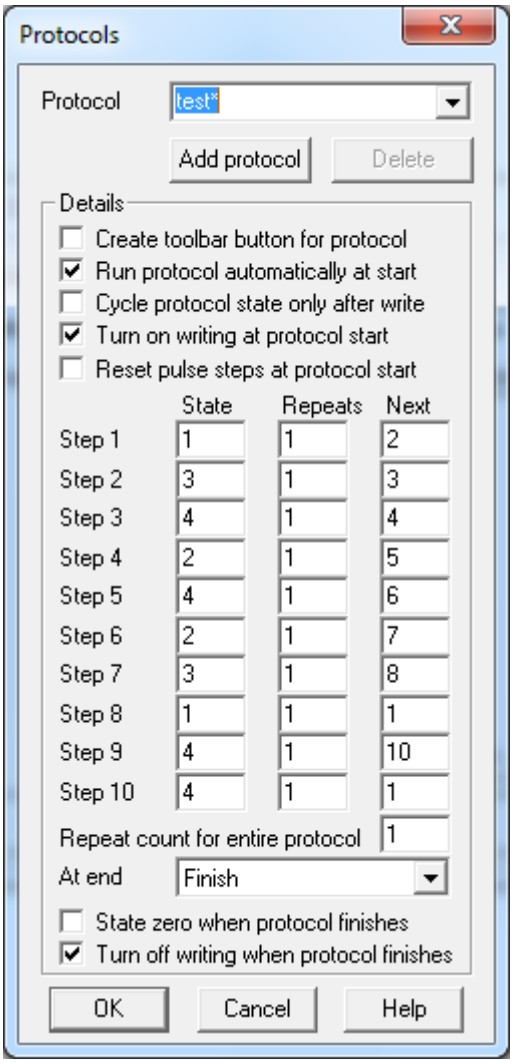

Pulses configuration
DIG
2
1
0
0.00 s
30.00
Del
Copy
State 4
Label
>>
Pulse train DIG 1 at 2.60 to 27.98 s
Id
Start (s)
2.6
Pulses
40
Length (s)
0.03
Interval (s)
0.65
Freq (Hz)
1.53846
OK
Cancel
Help


Parameters - C:\Tapping\RUN1.SGC
General
Port setup
Outputs
States
Automate
State variation
Dynamic outputs
Ordering
Protocol
Number of extra states
4
Protocols ...
Magstim ...
OK
Cancel
Run now
Help

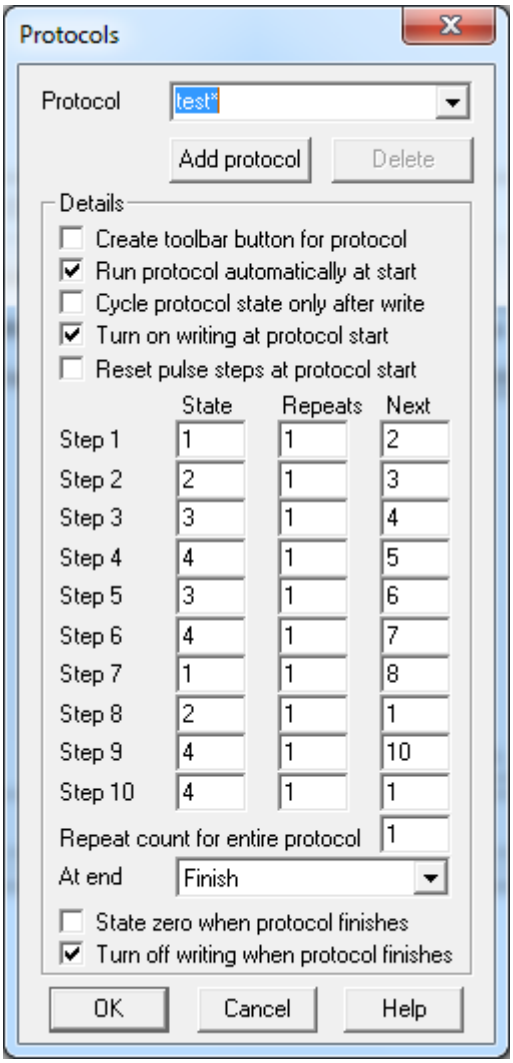

Protocols
Protocol
test*
Add protocol
Delete
Details
Create toolbar button for protocol
Run protocol automatically at start
Cycle protocol state only after write
Turn on writing at protocol start
Reset pulse steps at protocol start
State
Repeats
Next
Step 1 2 1 2
Step 2 1 1 3
Step 3 3 1 4
Step 4 4 1 5
Step 5 1 1 6
Step 6 4 1 7
Step 7 3 1 8
Step 8 2 1 1
Step 9 4 1 10
Step 10 4 1 1
Repeat count for entire protocol
1
At end
Finish
State zero when protocol finishes
Turn off writing when protocol finishes
OK
Cancel
Help


Parameters - C:\Tapping\RUN1.SGC
General
Port setup
Outputs
States
Automate
Filing
Path
C:\Tapping\TappingDATA
Browse ...
File name template
S1_000
>>
Save file to disk on sampling finish
Sampling limits
Number of frames
8
Sampling duration (s)
60
File size (KByte)
1
Artefact reject ...
OK
Cancel
Run now
Help

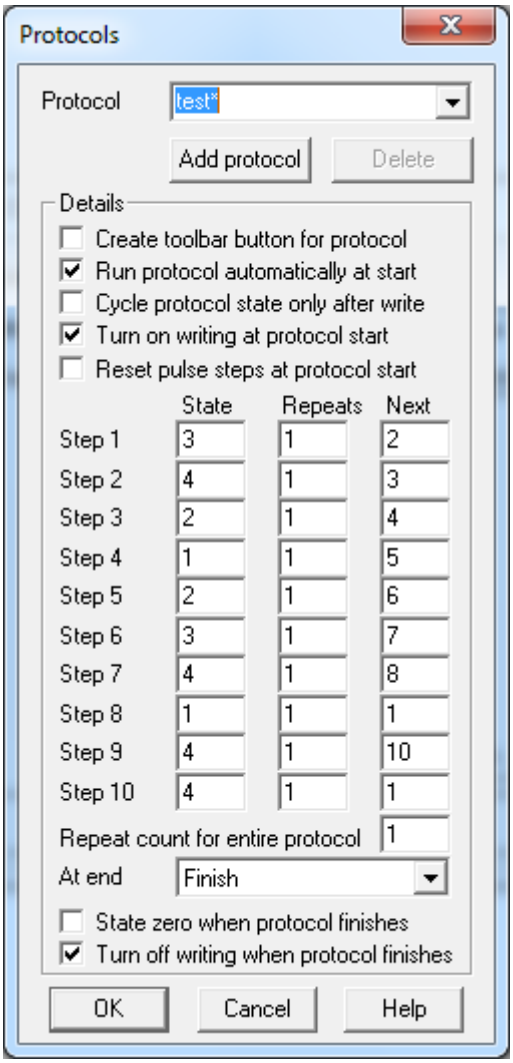
RUN 2


Protocols
Protocol
test*
Add protocol
Delete
Details
Create toolbar button for protocol
Run protocol automatically at start
Cycle protocol state only after write
Turn on writing at protocol start
Reset pulse steps at protocol start
State
Repeats
Next
Step 1 1 1 2
Step 2 3 1 3
Step 3 4 1 4
Step 4 2 1 5
Step 5 4 1 6
Step 6 2 1 7
Step 7 3 1 8
Step 8 1 1 1
Step 9 4 1 10
Step 10 4 1 1
Repeat count for entire protocol 1
At end
Finish
State zero when protocol finishes
Turn off writing when protocol finishes
OK
Cancel
Help

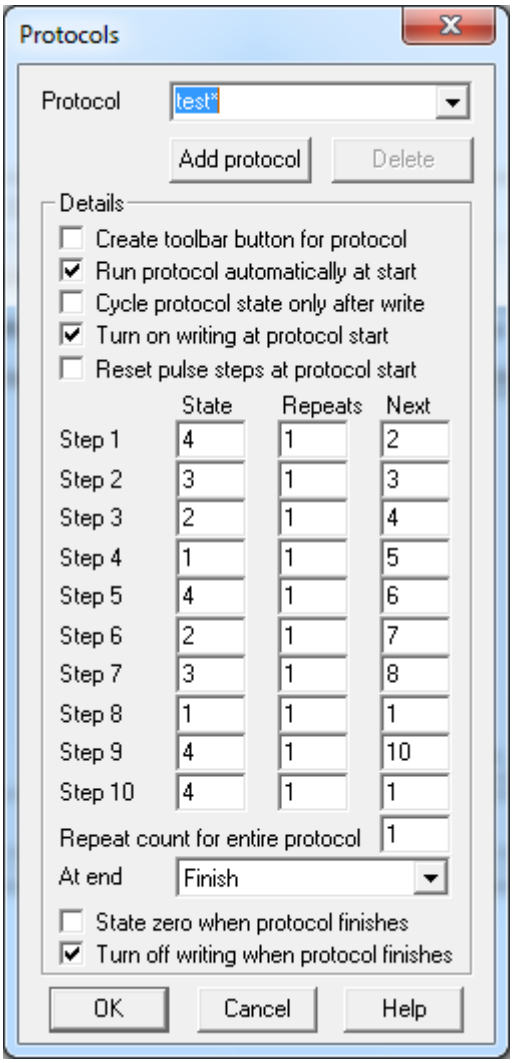
RUN 3


Protocols
Protocol
test*
Add protocol
Delete
Details
Create toolbar button for protocol
Run protocol automatically at start
Cycle protocol state only after write
Turn on writing at protocol start
Reset pulse steps at protocol start
State
Repeats
Next
Step 1 1 1 2
Step 2 2 1 3
Step 3 3 1 4
Step 4 4 1 5
Step 5 3 1 6
Step 6 4 1 7
Step 7 1 1 8
Step 8 2 1 1
Step 9 4 1 10
Step 10 4 1 1
Repeat count for entire protocol 1
At end
Finish
State zero when protocol finishes
Turn off writing when protocol finishes
OK
Cancel
Help

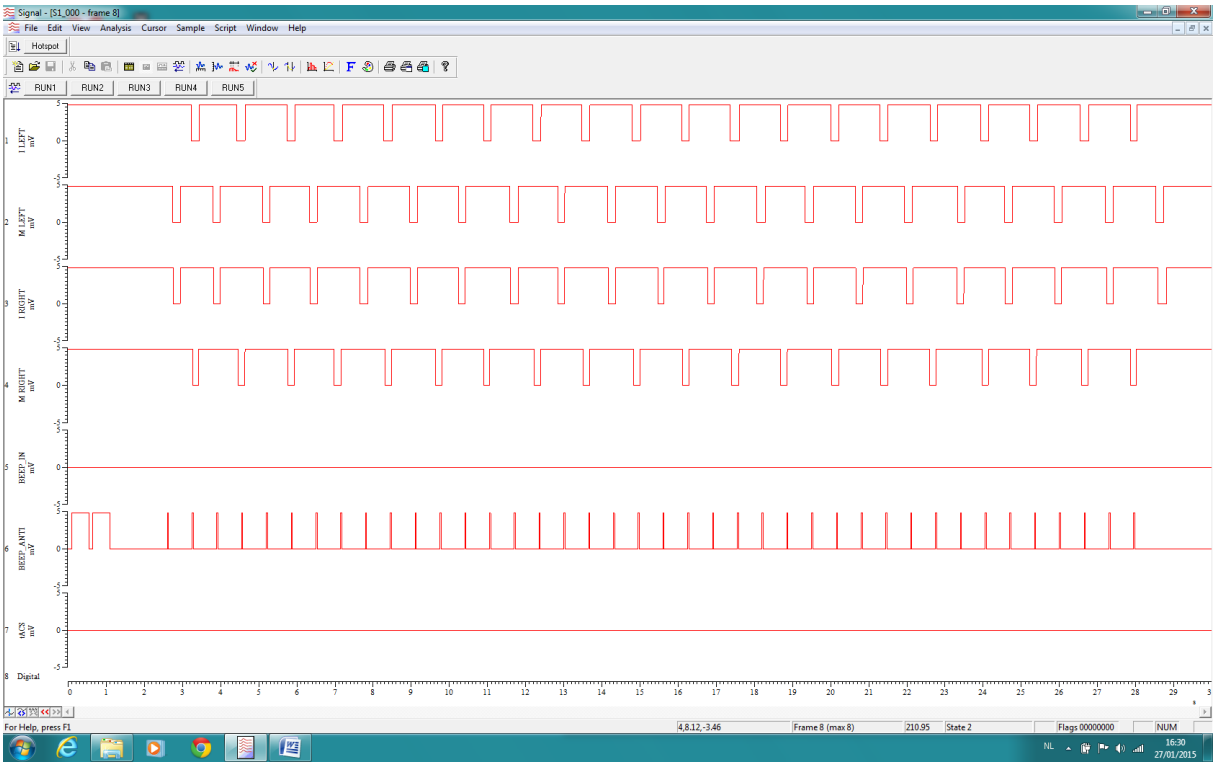
RUN 4


Protocols
Protocol
test*
Add protocol
Delete
Details
Create toolbar button for protocol
Run protocol automatically at start
Cycle protocol state only after write
Turn on writing at protocol start
Reset pulse steps at protocol start
State
Repeats
Next
Step 1 3 1 2
Step 2 4 1 3
Step 3 2 1 4
Step 4 1 1 5
Step 5 2 1 6
Step 6 3 1 7
Step 7 4 1 8
Step 8 1 1 1
Step 9 4 1 10
Step 10 4 1 1
Repeat count for entire protocol 1
At end
Finish
State zero when protocol finishes
Turn off writing when protocol finishes
OK
Cancel
Help

RUN 5

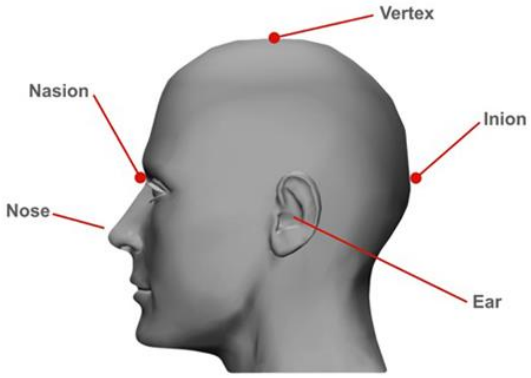

Protocols
Protocol
test*
Add protocol
Delete
Details
Create toolbar button for protocol
Run protocol automatically at start
Cycle protocol state only after write
Turn on writing at protocol start
Reset pulse steps at protocol start
State
Repeats
Next
Step 1 4 1 2
Step 2 3 1 3
Step 3 2 1 4
Step 4 1 1 5
Step 5 4 1 6
Step 6 2 1 7
Step 7 3 1 8
Step 8 1 1 1
Step 9 4 1 10
Step 10 4 1 1
Repeat count for entire protocol 1
At end
Finish
State zero when protocol finishes
Turn off writing when protocol finishes
OK
Cancel
Help

Voorbeeld


Signal - [S1_000 - frame 8]
File Edit View Analysis Cursor Sample Script Window Help
Hotspot
RUN1 RUN2 RUN3 RUN4 RUN5
I LEFT mV
M LEFT mV
I RIGHT mV
M RIGHT mV
BEEP_IN mV
BEEP_ANTI mV
ACS mV
Digital
For Help, press F1
4,8.12,-3.46
Frame 8 (max 8)
210.95
State 2
Flags 00000000
NUM
NL
16:30
27/01/2015

Stappenplan elektrodenplaatsing + instellingen stroomapparaat

1. Sponsjes nat maken met NaCl 0.9%. Sponsjes lichtjes uitwringen.
2. Elektrodes voorzichtig in sponsjes steken. De elektrodes eerst goed nakijken, er mogen GEEN scheurtjes in zitten (anders gevaar op brandwonden).
3. Kabeltje voorzichtig in sponsje steken (anders gevaar op scheuren)
4. Op hoofd aanbrengen met de onderkant op het hoofd. Onderkant = volledig vlakke kant.
5. 1 elektrode op linker motorische cortex: 25cm² en 1 elektrode op rechter motorische cortex: 50cm²
6. Met meetlint afstand bepalen tussen nasion (tussen 2 ogen) en inion (knobbeltje vanachter op het hoofd). Bv 37 cm



Alexandre F. DaSilva1, Magdalena Sarah Volz2,3, Marom Bikson4, Felipe Fregni2, 2011

7. Midden nemen van afstand tussen nasion en inion. Hier een puntje tekenen (om dit punt terug te vinden) Bv 37/2=18.5cm
8. Met meetlint afstand bepalen tussen 2 oren (om het gemakkelijker te maken de proefpersoon 2 vingers in de oren laten steken). Bv 36cm
9. Midden nemen van afstand tussen 2 oren. Hier een puntje tekenen (om dit punt terug te vinden) Bv 36/2=18cm
10. Vertix bepalen (= kruispunt van deze 2 punten)
11. Linker motorische cortex bepalen = 1/3 naar beneden van afstand van vertex tot linker oor. Hier een puntje tekenen (om dit punt terug te vinden) Bv 18cm van vertex tot oor: 18/3= 6 dus 6cm naar beneden gaan
12. Rechter motorische cortex bepalen op dezelfde manier
13. Rubbere banden bevestigen, zien dat deze strak genoeg zitten, maar ook niet te strak. FOTO (Je kan verschillende banden bevestigen, je moet er alleen voor zorgen dat de sponsjes op hun plaats blijven)
14. Sponsjes onder rubbere banden steken en haren zoveel mogelijk opzij doen. (gemakkelijkste voor proefpersoon met de kabels naar achteren)
15. Kabels aansluiten (juiste kleuren)
16. Apparaat opzetten en kijken hoeveel batterij het nog heeft
17. Study NO
18. Parameters instellen:
    a. Sinus (NIET sinus (hw)
    b. Current= 1000µA = 1mA
    c. Offset= 0

   d. Frequentie= 10Hz of 20Hz (rechter bovenknop ingedrukt houden om tot bepaalde frequentie te komen)
   e. Fase= 0
   f. Cycles = 250x 2π (voor 10Hz) en 500x 2π (voor 20Hz). (1cycle = 1 keer op en neer gaan)
   g. Trigger cycle= 1x 2π
   h. Fade in out= 1
19. Stroom opzetten: naar parameter gaan, op rechter bovenknop drukken
20. Stimulation YES or NO: NO
21. Trigger input= repetitive
22. Trigger output= disable
23. Naar parameter gaan: stimulation YES or NO: YES (25 seconden stimuleren)
24. Als impedantie te hoog is, meer NaCl op de sponsjes doen (machientje gaat geen stroom geven, dit is boven 55kohm) of gel onder elektrode doen
25. Eerst stroom geven zonder trigger van geluid en vragen of alles oke is bij de patient
26. Taak ook laten doen om te oefenen
27. Eerste trigger is 1 of 2 biepjes
   a. 1 biepje = infase (L: wijsvinger R: wijsvinger) (gemakkelijk)
   b. 2 biepjes = antifase (L: wijsvinger R: middenvinger) (moeilijker)
28. Patient moet dit 5 blokken doen van elk 4 minuten
29. Patient moet gelijk aan de biepjes de toetsen indrukken, met linker en rechter hand zo gelijk mogelijk drukken
30. Patient krijgt het scherm of stimulatie apparaat niet te zien
31. Starten: RUN 1 → starten → finish → RUN 2 → starten → finish enz…
32. Einde test: alles van hoofd halen, kabeltjes voorzichtig uit sponsjes halen en GOED afspoelen met water.
33. Machientje afzetten en kabels uittrekken
34. ’s avonds opladen

Opslaan als tekstdocument

file openen (met golfjes)

1. export as
2. opslaan in juiste map , in dit geval pilot laura
3. save as type: text file
4. naam: (voor eerste:) S1_1
5. text output cofiguration: OK
6. export from S1_002: frames: ALL FRAMES : export

Appendix 2: Informed consent

INFORMATIE- EN TOESTEMMINGSFORMULIER

Project titel: THE INFLUENCE OF TRANSCRANIAL ALTERNATING CURRENT STIMULATION (TACS) ON MOTOR CONTROL EN MOTOR PERFORMANCE

Nederlandstalige project titel: De invloed van transcraniële alternerende stroom stimulatie op motorische controle en motorische prestatie.

Beste kandidaat deelnemer,

Als u besluit om aan deze studie deel te nemen, moet u hiermee eerst schriftelijk instemmen. Het door u ondertekende toestemmingformulier wordt door het onderzoeksteam bewaard. U zal een kopie van deze informatiebrochure en uw ondertekend toestemmingsformulier ontvangen om te bewaren. Om u een goed beeld te geven van de onderzoeksprocedure is het van belang dat u de onderstaande informatie goed begrijpt. Indien deze informatiebrochure echter informatie bevat die u niet begrijpt, zijn wij uiteraard graag bereid om deze te verklaren.

Achtergrondinformatie

Om bepaalde motorische taken succesvol uit te voeren is gebleken dat hersengebieden synchrone of asynchrone hersengolven produceren. Uit recent onderzoek is gebleken dat Transcraniële (= door de schedel) alternerende stroom stimulatie kan gebruikt worden om hersengolven in verschillende hersengebieden makkelijker te synchroniseren of te desynchroniseren. Wat hiervan de implicaties zijn op motorische controle en motorische prestatie is echter nog onduidelijk.

Doel van het onderzoek

In deze studie willen we nagaan of tACS een invloed heeft op het uitvoeren van een bimanuele taak Bij deze taak wordt aan de deelnemers gevraagd om een ritmisch patroon te produceren met de wijsvinger en de middelvinger van zowel de linker- als de rechterhand gelijktijdig. We willen bestuderen of tACS een invloed heeft op de motorische controle (uitvoering van het ritmisch patroon).

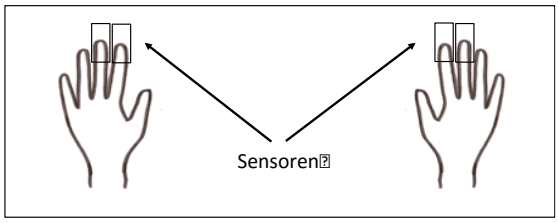
Omschrijving van het onderzoek

Gegevensverzameling

Vooraleer het onderzoek gestart wordt, zal iemand van het onderzoeksteam u een aantal vragenlijsten laten invullen met betrekking tot het onderzoek. U zal ook gescreend worden om te zien of u in aanmerking komt voor het onderzoek.

Metingen

Uw motorische prestatie zal gemeten worden met een fingertapping taak (zie figuur). U zal gevraagd worden om een ritmisch patroon te produceren met de wijsvinger en de middelvinger van zowel de linker- als de rechterhand gelijktijdig. Het doel is om de toetsen links en rechts zo gelijktijdig mogelijk in te drukken. De snelheid waarmee dit patroon dient worden uitgevoerd zal aangegeven worden door een metronoom (biep-signaal).



Fingertapping taak: De wijs- en middelvingers van de linker en de rechterhand maken contact met een sensor (1 sensor per vinger). Een metronoom geeft het ritme aan. Twee verschillende patronen worden aangeboden: in-fase tapping en anti-fase tapping. Bij in-fase tapping moeten beide wijsvingers (of middelvingers) gelijktijdig de sensor aanraken. Bij anti-fase tapping moeten de wijsvinger van de linkerhand en de middelvinger van de rechterhand (of omgekeerd) gelijktijdig de sensor aanraken.

tACS

Met Transcraniële Alternating Current Stimulation (tACS) wordt een microstroom aangebracht op het hoofd. De tACS stimulator bestaat uit een doos (unit met display en batterij) en 2 spons elektroden. Deze elektroden worden op het hoofd bevestigd. Let op, uw hoofd kan dus een beetje nat worden. Deze niet-invasieve stimulatie kan een prikkelende sensatie veroorzaken op het hoofd. Het is ook mogelijk dat u tijdens de stimulatie een lichte flikkering in het gezichtsveld waarneemt.

Duur van het onderzoek

Het experiment zal worden uitgevoerd in 3 afzonderlijke sessies met een interval van minimum 24 uur tussen elke sessie. We streven ernaar om elke meting op hetzelfde uur te starten. We verwachten dat elke sessie maximum 1 uur in beslag zal nemen. Uiteraard voorzien we extra tijd om al uw vragen te beantwoorden. Elke sessie zal identiek verlopen. Het enige verschil is dat de parameters van de microstroom en/of de stimulatie locatie zullen wijzigen.

1. De elektroden worden bevestigd op uw hoofd.
2. Vervolgens starten we het experiment. Tijdens het experiment kan u op verschillende momenten gestimuleerd worden tijdens het uitvoeren van de taak. Dit experiment zal bestaan uit 5 blokken van 4 minuten met telkens een pauze van anderhalve minuut.

Risico's verbonden aan deze studie

Er zijn weinig of geen risico's verbonden aan deze studie. tACS kan een sensorische sensatie (tinteling) en/of een lichte flikkering in het gezichtsveld veroorzaken. In zeer uitzonderlijke gevallen kan er een brandwonde/etsing van de huid optreden (bij een defecte elektrode).

Criteria waardoor u ongeschikt wordt bevonden voor deze studie:

- Linkshandig
- (medische) conditie die maakt dat de arm/handfunctie verstoord (abnormaal) is
- Metaal in het hoofd
- Pacemaker / Draden / Implanteerbare defibrillator
- Metalen kunstklep
- Coronaire bypass – clips
- Biostimulator of TENS-apparaat
- Aneurysmaclips (hersenbloedvaten, aorta, etc.)
- Intracraniële clips (metalen clips die operatief binnen de schedel werden aangebracht)
- Middenoor prothese (heelkunde van de gehoorsbeentjes)

- Andere prothesen of orthesen (indien metaal)
- Geïmplanteerde medicatiepomp
- Granaatscherven (eender waar in het lichaam)
- Metaalarbeider geweest in het verleden
- Eén van volgende aandoeningen gehad in het verleden:
    - ✓ Hersentrombose
    - ✓ Hersenbloeding
    - ✓ Hoofdtrauma
    - ✓ Meningitis (hersenvliesontsteking)
    - ✓ Hartaanval
    - ✓ Lange periode van bewusteloosheid (meer dan 1 uur)
    - ✓ Migraine
    - ✓ Epilepsie
- Voorgeschiedenis van hersenchirurgie
- Familiale voorgeschiedenis van therapieresistente epilepsie
- Voorgeschiedenis van actief misbruik van een bepaalde stof gedurende het laatste jaar
- Mogelijke zwangerschap

Voordeel voor uzelf als deelnemer

Er zijn geen directe voordelen verbonden aan deelname aan deze studie. Door deel te nemen aan deze studie draagt u uw steentje bij aan de wetenschap. De resultaten kunnen fundamentele inzichten geven met betrekking tot de het sensorimotorische systeem en kunnen op termijn tot nieuwe revalidatie strategieën leiden voor patiënten die problemen hebben met sensorische problemen en/of motorische controle. Nadat de resultaten van deze studie geanalyseerd en verwerkt zijn, zal u indien u dit wenst uitgebreid geïnformeerd worden over onze bevindingen.

Vergoeding

U zal een kleine vergoeding krijgen voor uw deelname aan de studie, nl. een cinematicket of een boekenbon (U kan zelf kiezen wat u verkiest). Deze ontvangt u nadat u alle sessies voltooid hebt.

Verzekering

In het kader van deze studie werd er een verzekering afgesloten. Conform de Belgische wet van 7 mei 2004 inzake experimenten op de menselijke persoon, is de opdrachtgever zelfs foutloos, aansprakelijk voor alle schade die de deelnemer of zijn rechthebbenden opliepen en die rechtstreeks dan wel onrechtstreeks verband vertoont met het experiment. De opdrachtgever van deze studie [KU Leuven/Universiteit Hasselt] heeft een verzekering afgesloten die deze aansprakelijkheid dekt. Indien U schade zou oplopen ten gevolge van uw deelname aan deze studie zal die schade bijgevolg worden vergoed conform de Belgische wet van 7 mei 2004.") evenals de informatie over de vertrouwelijkheid (vertrouwelijk behandelen van de gegevens die in het kader van de studie verzameld worden; het medisch geheim, de internationale richtlijnen (ICH-GCP) en de Belgische wetgeving; codering van de studiegegevens).

Vertrouwelijkheid

Zoals alle medische gegevens worden ook de gegevens die in het kader van de studie verzameld worden uiterst vertrouwelijk behandeld. Hierbij worden het medisch geheim, de internationale richtlijnen (ICH-GCP) en de Belgische wetgeving nageleefd (onder meer de wettelijke vereisten zoals bepaald in de Belgische Wet van 8 december 1992 inzake bescherming van de persoonlijke levenssfeer en de Belgische Wet van 22 augustus 2002 inzake rechten van de patiënt).

Deelname aan de studie

Deelname aan deze studie is geheel vrijwillig. Indien u toestemt om aan deze studie deel te nemen, verzoeken we u wel om zo goed mogelijk het voorgeschreven protocol op te volgen. U kan op elk ogenblik van de studie signaleren dat u het onderzoek wil onderbreken.

Terugtrekken uit de studie

U heeft het recht om de deelname aan deze studie **op elk moment** stop te zetten zonder enige verplichting tot verdere verantwoording.

Het onderzoeksteam kan zonder uw toestemming u uit het onderzoek terugtrekken en bijgevolg het registreren van de gegevens stopzetten in de volgende gevallen:

- U houdt zich niet aan het onderzoeksprotocol.
- U neemt deel aan een ander onderzoek.

Goedkeuring onderzoek en toestemmingsformulier

Dit onderzoek werd goedgekeurd door de Commissie Medische Ethiek van het UZ Leuven op datum van 25/08/2014 en door de lokale Commissie Medische Ethiek van de UHasselt op datum van 5/12/2014. Nadat u deze informatie heeft gelezen, kan u steeds bijkomend vragen stellen aan de verantwoordelijke onderzoekers. Wanneer u voldoende bedenktijd heeft gehad, wordt u gevraagd om te beslissen over deelname aan dit onderzoek. U kan de beslissing reeds nemen bij de toelichting van het onderzoek of na enkele dagen. Indien u toestemming tot deelname geeft, dient u het bijbehorende toestemmingsformulier te ondertekenen. U krijgt een kopie van deze informatie en van het getekende toestemmingsformulier indien u besluit mee te doen. Dit handtekeningenblad kan u na het krijgen van de toelichting afgeven. U kan het ook opsturen naar het volgende adres, maar wel binnen de week na het toelichten van het onderzoek:

Dr. Koen Cuypers
Motor Control Laboratory
Movement Control and Neuroplasticity Research Group
KU Leuven
Tervuurse Vest 101
3001 Leuven

Vragen

Mocht u naar aanleiding van deze informatiebrochure nog vragen hebben, kan u steeds terecht bij Dr. Koen Cuypers (☎ +32 479 43 36 46), Laura Van den Bergh (☎ +32 472 76 26 86), Stefaan Vreys (☎ +32 494 47 76 19).

Onderzoekers

Dr. Koen Cuypers, Laura Van den Bergh, Stefaan Vreys

INFORMATIE- EN TOESTEMMINGSFORMULIER

Project titel: De invloed van transcraniële alternerende stroom stimulatie op motorische controle en motorische prestatie.

GEEF AAN WAT VAN TOEPASSING IS

1. Heeft U de informatie bundel mbt deze studie gelezen? JA/NEEN
2. Heeft U de mogelijkheid gehad om vragen te stellen mbt deze studie? JA/NEEN
3. Heeft men al Uw vragen voldoende kunnen beantwoorden? JA/NEEN
4. Heeft U voldoende informatie over deze studie gehad? JA/NEEN
5. Met wie heeft U over deze studie gesproken? Naam:_____
6. Begrijpt U dat U vrij bent om Uw deelname aan deze studie stop te zetten
   *Op elk moment JA/NEEN
   *Zonder een rede van stopzetting op te geven JA/NEEN
7. Gaat U akkoord om aan deze studie deel te nemen? JA/NEEN
8. Zijn er exclusiecriteria op U van toepassing waardoor U ongeschikt wordt bevonden om deel te nemen aan deze studie (zie pagina 2)? JA/NEEN

Handtekening deelnemer:_____ Datum: _____

Naam Deelnemer (blok letters):_____

De onderzoeker verklaart dat mijn persoonlijke informatie enkel zal gebruikt worden in functie van deze studie en niet voor andere doeleinden. Deze informatie wordt strikt vertrouwelijk behandeld overeenkomstig artikel 7 en volgens de 'Wet op het privéleven met betrekking tot de behandeling van persoonlijke gegevens' van 8 december 1992.

Handtekening onderzoeker:_____

Naam onderzoeker:_____

Appendix 3: List of abbreviations

EEG:	Electroencephalography
HF tRNS:	High frequency transcranial random noise stimulation
LF tRNS:	Low frequency transcranial random noise stimulation
MEPs:	Motor evoked potentials
RCT:	Randomized controlled trial
S1:	Somatosensory cortex
STDP:	spike-timing-dependent plasticity
tACS:	Transcranial alternating current stimulation
tDCS:	Transcranial Direct current stimulation
TMS:	Transcranial magnetic stimulation

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Auteursrechtelijke overeenkomst

Ik/wij verlenen het wereldwijde auteursrecht voor de ingediende eindverhandeling:
The effect of 10Hz and 20Hz transcranial alternating current stimulation on the synchronization of bimanual finger tapping

Richting: **master in de revalidatiewetenschappen en de kinesitherapie-revalidatiewetenschappen en kinesitherapie bij kinderen**
Jaar: **2016**

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Voor akkoord,

Van Den Bergh, Laura **Vreys, Stefaan**

Datum: **14/06/2016**