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Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

The effects of aging on transcranial alternating current stimulation during a bimanual tracking task

Myrthe Lousbergh
Tine Louwet

Scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie, afstudeerrichting revalidatiewetenschappen en kinesitherapie bij kinderen

PROMOTOR :

Prof. dr. Raf MEESEN

BEGELEIDER :

Mevrouw Stefanie VERSTRAELEN

De heer Sybren VAN HOORNWEDER

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Foreword

To complete the education of physiotherapy and rehabilitation sciences at the University of Hasselt this master's thesis was made. The authors would like to thank a few people for participating in the production of this master's thesis.

First of all, we would like to thank our promotor Prof. Dr. Raf Meesen and our copromotor Dr. Kim Van Dun. Moreover, we would like to thank Dra. Stefanie Verstraelen and Drs. Sybren Van Hoornweder for guiding us during the process of making a master's thesis and for giving us constructive feedback. Also, that we were allowed to be a part of their PhD study.

We would like to thank the group 'Masterproef Neuroplasticity and Neurorehabilitation' to help us with gathering participants and data for our study and help us acquire the necessary data.

To finish, we would like to thank the participants for participating in this study. We would like to thank them for making time for us to take the measurements and cover this distance, despite the fact that no compensation is attached to this study.

And last but not least we would like to thank each other for the nice cooperation. We worked on this thesis with a critical view. On top of that we were well attuned to each other.

Diepenbeek, 2021 M.L. en T.L

Situation

This research is situated in the neurological and neurorehabilitation domain. More specifically, it focusses on non-invasive brain stimulation (NIBS). This study takes place in the Rehabilitation sciences of neurological revalidation. The study will be supervised by the Neurologic Rehabilitation research group and is part of Stefanie Verstraelen's doctoral study. Within the construct NIBS, different techniques exist. Transcranial direct current stimulation (tDCS) impacts the polarization of the cortical neurons using direct current. Transcranial alternating current stimulation (tACS), on the other hand uses an alternating sinusoidal current to interact with the natural cortical oscillations of the brain. Transcranial random noise stimulation (tRNS) is a particular form of tACS that varies the current intensity and frequency in a randomized manner (Yasuto Inukai et al., 2016). tACS may entrain endogenous neural oscillations in a frequency- and phase-specific manner. The frequency of the applied field is typically matched to the frequency of the intrinsic frequency of the target activity or target region (Bland, Sale, 2019). With tACS the stimulation can be done over larger brain areas than with other stimulation forms like tDCS.

This study aims to find whether or not there is a difference in outcome between older and younger adults by using tACS in a bimanual task. The outcome is the accuracy of the task, described with average trace deviation and average target deviation. This study will be done with healthy participants to find out whether or not there are beneficial effects in healthy participants. When positive effects are found in this present study, further studies will be necessary to implement these findings in participants with neurological disorders.

The research questions are drawn up by ourselves aligned with our previous literature study and the existing protocol for this experiment.

The recruitment of the participants was already partially done due to the current project being an ongoing investigation. We therefore, only have a partial share in the further recruitment together with fellow students who also carried out their master's thesis with the same supervisors. The same applies to data acquisition.

This study was written according to the instructions of the central format. It was a duo master's thesis, in which both researchers had an equal share. The entire writing process was done by ourselves, with feedback from the supervisors.

References:

Bland, N.S., Sale, M.V. (2019) Current challenges: the ups and downs of tACS. Exp Brain Res. 2019 Dec;237(12):3071-3088. doi: 10.1007/s00221-019-05666-0. Epub 2019 Oct 16.

Yasuto Inukai, Kei Saito, Ryoki Sasaki, Shota Tsuiki, Shota Miyaguchi, Sho Kojima, et al. (2016) Comparison of Three Non-Invasive Transcranial Electrical Stimulation Methods for Increasing Cortical Excitability. Front Hum Neurosci. 2016; 10: 668. Published online 2016 Dec 27. doi: 10.3389/fnhum.2016.00668

The effects of aging on transcranial alternating current stimulation during a bimanual tracking task.

1. Abstract

Background: tACS is a non-invasive brain stimulation technique that influences endogenous brain oscillations. It has the potential to positively impact bimanual motor tasks, which are an intrinsic part of daily life. Stimulation over the dorsolateral prefrontal cortex (DLPFC) and the posterior parietal cortex (PPC) could improve the performance of a spatial working memory task and motor learning.

Objectives: One experiment where theta oscillations were used on the two brain areas to improve a bimanual tracking task (BTT).

Participants: In this experiment, 46 healthy participants (31 young adults and 15 older adults) were randomized into three groups (in-phase, antiphase and sham stimulation) for the young adults and two groups (in-phase and antiphase stimulation) for the older adults.

Measurements: The study focused on the quality of the BTT task. This was measured by average trace deviation and average target deviation.

Results: No significant effect was found for the form of stimulation. For the quality of performance across blocks, a significant effect was usually found. There was a significant improvement over time. The last difference measured was between the two ages groups, which was also significant where the younger group scored better.

Conclusion: The research questions were not answered as expected. Stimulation form was never significant, whereas age was significant. For further and more comprehensive research, new studies should be conducted. In which the stimulated brain regions may or may not be modified as well as the stimulation frequency.

Keywords: 'transcranial alternating current stimulation', 'tACS', 'bimanual tracking task', 'younger adults, 'elderly adults'

2. Introduction

Within the motor tasks of the upper limb, one can differentiate between unimanual and bimanual motor tasks. Bimanual motor tasks are required in most actions of daily living. As a result, the decline of bimanual motor task has an important impact on daily living and impairs the quality of life (Fusco et al., 2012).

As a result of aging, the performance of motor tasks declines which is linked to changes in the brain. More specifically, the process of aging is associated with cortical hyperactivity in networks which play a role in attention-driven processes and motor processes in both unimanual and bimanual motor tasks and subcortical hypoactivity during bimanual tasks. In addition to changes in activation in local areas, the interaction between distributed brain areas also exhibits age-related effects, i.e. functional connectivity is increased in the resting-state brain as well as during task performance. (Larivière, et al., 2019)

On a different note, motor learning is the set of processes associated with practice or experience, which lead to a relatively permanent change in skilled motor performance (Schmidt, 1976). Studies report that the process of aging is associated with a decline of motor learning. Motor skills are learned at a slower rate and to a lesser extent when compared to younger adults (King, Fogel, Albouy, Doyon, 2013; Raz, Williamson, Gunning-Dixon, Head, Acker, 2000; Roig, Ritterband-Rosenbaum, Lundbye-Jensen, Nielsen, 2014; Seidler, 2006).

One type of motor learning is sensorimotor adaptation. In sensorimotor adaptation, participants must adapt their movements based on either sensory input or motor output. Visuomotor adaptation is a specific form of sensorimotor adaptation and relies more on the visual system. Moreover, according to Smith et al. two, overlapping, stages can be observed during motor learning: a cognitively driven early stage, characterized by rapid performance and an autonomous late learning stage which is characterized by smaller and slower performance gains (Smith et al., 2006; Keisler & Shadmehr, 2010). Spatial working memory also has an impact on motor learning. Anguera et al. (2010) investigated whether individual differences in spatial working memory capacity related to the speed of adaptive performance changes in a visuomotor adaptation paradigm. They found that the positive effects were specific to both the early period and spatial working memory. Thus for motor learning the early period and spatial working memory are required. Furthermore, they noted that there were overlapping areas in the brain in the early phase of motor learning during performance of a spatial working memory task and learning in the early phase. Specifically, the right dorsolateral prefrontal cortex (DLPFC) and the bilateral inferior parietal lobules (BIPL) were observed to be active (Anguera et al., 2010). Other studies substantiate the finding that in the early stage of motor learning, DLPFC and parietal regions are active. In the late stage of motor learning this activation shifts towards left premotor and right cerebellar regions. (Krebs et al., 1998;

Shadmehr & Holcomb, 1997; Graydon et al., 2005; Imamizu et al., 2000; Inoue et al., 2000; Krakauer et al., 2004; Miall et al., 2001). In sum, these findings suggest that the role of DLPFC is important in the process of motor learning.

In a study with elderly participants, Seidler, Bo and Anguera (2012) observed a lack of correlation between the rate of early adaptation and spatial working memory performance. Also in older adults, similar brain activation patterns were observed for a spatial working memory task performance compared to younger adults: i.e., the right DLPFC and bilateral inferior parietal. In contrast to young adults, older people did not show neural activation that overlapped with the early adaptation period, suggesting that spatial working memory in older adults works less efficiently (Anguera et al.,2011).

Transcranial alternating current stimulation (tACS) is a type of non-invasive brain stimulation characterized by application of an alternating sinusoidal current through electrodes to modulate neural oscillations. Oscillatory brain activity can be classified into five frequency bands: delta (< 4 Hz), theta (4-8 Hz), alpha (8-12 Hz), beta (13-30 Hz) and gamma (> 30 Hz). Each frequency has been linked to numerous functions (Miyaguchi et al., 2018). Several studies investigated the effects of the frequency bands in relationship to various body functions. tACS can be applied through multiple electrodes over two brain regions simultaneously, which is referred to as dual site tACS (Saturino, Madsen, Siebner, 2017). Dual-site tACS is typically either in-phase or anti-phase. In-phase is used when the stimulation of the two brain regions is synchronized (i.e., relative phase difference = 0 degrees) and aims to promote coupling of the targeted structures to facilitate information transfer (Polania et al., 2012; Reinhart, Nguyen, 2019). On the contrary, anti-phase stimulation is characterized by opposing induced waves in two cortical target areas (i.e., relative phase difference = 180 degrees) (figure 1). Sham stimulation is used to assess the efficacy of active stimulation and placebo effects. It imitates the cutaneous sensations of active stimulation to prevent placebo effects (Dissanayaka, Zoghi, Farrel, Egan & Jaberzadeh, 2017).

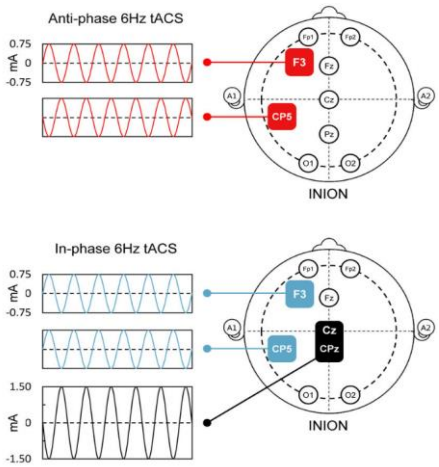

***Fig1**. In- and anti-phase stimulation.*

A previous tACS study, using 10, 50 and 300 Hz, showed that cerebellar interneural network may influence motor performance (Naro et al., 2017). Another region that could be stimulated is the dorsolateral prefrontal cortex together with the posterior parietal cortex (PPC) as aforementioned. An example is the study where the theta frequency band was used and they found evidence that tACS can modulate adaptive mechanisms of the cognitive control network, suggesting midfrontal theta oscillations as causally involved in cognitive control (Lehr, Henneberg, Nigam, Paulus & Antal, 2019).

To summarize: the purpose of the current work is to investigate if in- or anti-phase tACS could improve motor skills in bimanual motor tasks by stimulating the DLPFC-PPC. The difference in performance of a bimanual motor task was compared between younger and older adults, while they received either in-phase/anti-phase tACS or sham stimulation. A bimanual tracking task was used to assess bimanual motor learning. If in-phase or anti-phase tACS stimulating the DLPFC-PPC has a promoting effect in healthy older and younger people, it could be used as a rehabilitation tool. The additional questions for this study are: What are the differences in outcome between younger (18-30) and older (65-77) populations. Furthermore, we aim to unravel the different effects induced by in-phase versus anti-phase stimulation. Finally, the differences within elderly people between sham stimulation and tACS will be explored. We hypothesize that the modulation of DLPFC with in-phase tACS will improve bimanual motor tasks in both groups. Moreover we expect that the improvements can be seen by facilitating interregional information transfer between the targeted brain areas and hence also the performance in the elderly population compared to younger people. We expect that the stimulation will activate the regions of spatial working memory, because this was an important factor of motor learning. In elderly people there was a lack of activation in that region, so we hope to stimulate this area to activate the spatial working memory. Moreover, older adults exhibit deficits in visuomotor adaptation (Seidler, 2006; Bock, 2005) and have reduced spatial working memory performance (Reuter-Lorenz et al., 2001; Hale et al.,2011; Piefke et al., 2010).

3. Method section

3.1. Participants

This study included 31 younger adults (YA) (18-30 years) and 15 older adults (OA) (65-77 years). Participants were randomly divided into the stimulation groups. For the YA there were three groups (in-phase, anti-phase or sham). For the OA there were 2 groups (in-phase and anti-phase).

The inclusion criteria were being right-handed (measured by the Edinburgh Handedness Inventory (Oldfield 1971)), having normal cognitive functioning measured by the Montreal Cognitive Assessment (MoCA) questionnaire whereby a total score of 26/30 or higher is considered normal (Nasreddine et al. 2005; Carson, Leach, Murphy, 2017) and having a normal or corrected-to-normal vision.

The exclusion criteria in this study were the following: having contra-indications for Transcranial Electrical Stimulation (TES) (according to the TES screening questionnaire (Antal et al. 2017)), having a neurological disorder or a psychological history. Participants were also excluded when they had a physical limitation that made the execution of the bimanual task impossible. Furthermore, pregnant women and persons with drug, alcohol and/ or tobacco abuse were excluded. Lastly, persons who took medication that affects the central nervous system and/or who had a skin allergy to cosmetics or lotions were excluded as well.

This study was approved by the local ethical committee of UHasselt (Faculty of Medicine and Life Sciences, B9115201940316).

3.2. Procedure section

tACS

Dual-site tACS was applied using two stimulation devices (DC Stimulator plus, Eldith, neuroConn GmbH, Ilmenau, Germany), each connected to two customized rubber electrodes. Each pair of electrodes consisted of a center electrode of a 20 mm diameter and an open-ring electrode of 40 mm inner diameter and 60 mm outer diameter (Saturnino et al. 2017).

Participants received one of the two or three stimulation forms (in-phase, anti-phase or sham), which was pseudorandomized. The researchers, who took the measurement knew which stimulation form was used. Neither the researchers, who ran the statistics, nor the participants knew what form was used. One center-ring montage was placed over the right DLPFC and the other center-ring montage was placed over the right PPC. Stimulation intensity was set to 2 mA peak-to-peak, with a frequency of 6Hz (Figure 2) (Saturnino et al. 2017).


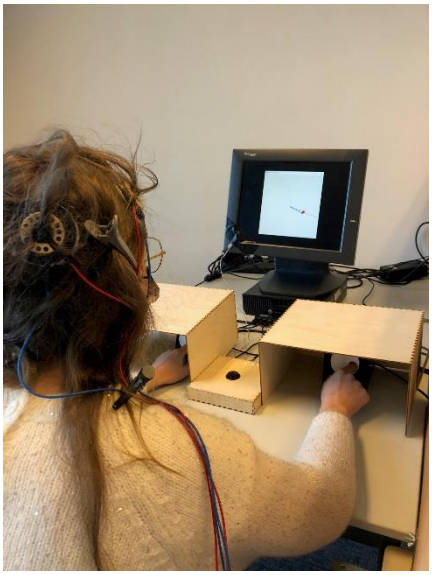

Fig 2. *Setup ring electrodes over DLPC and PPC*

Stimulation was applied for 20 minutes, during which the impedance was continuously monitored and kept below 6 Hz. An electrode gel was used to ensure optimal contact between skin/hair with the electrodes (TEN-20 paste, NeuroConn, Ilmenau, Germany). Stimulation was applied while performing the bimanual tracking task.

Bimanual Tracking Task

The bimanual task used in this study was a Bimanual Tracking Task (BTT) (adapted from Pauwels, Swinnen, Beets, 2014). This is a motor task during which participants were seated in a comfortable chair in front of a computer screen on which the task was displayed, with both forearms pronated on the table in front of them. The index finger of each hand controlled a dial of the response apparatus. By spinning the two dials with their index fingers, the participant could control a cursor on the screen. Spinning with the right index finger caused the cursor to move horizontally while the left index finger caused a vertical movement. The participants were instructed to track a white target dot, that moved at a constant speed over a straight line, that was displayed on the screen in front of them. This by spinning the two dials (figure 3). During the motor task, the participant was provided with online visual feedback, which was indicated by the distance traveled of the target was drawn as a red line. There were two varying parameters within each trial. For starters, there were two different inter-hand frequency ratios (1:3 and 3:1). This means that for example for the 1:3 ratio, the right index finger had to turn three times faster than the left finger. The second variable parameter was the quadrant wherein the line was displayed. There were four different quadrants, whereby in each quadrant only one condition was used (clockwise or counterclockwise) each index finger must be turned. This caused a total of 4 different task variants (1:3 isodirectional – right, 3:1 isodirectional - left, 1:3 non-isodirectional – outward, 3:1 non-isodirectional inward).

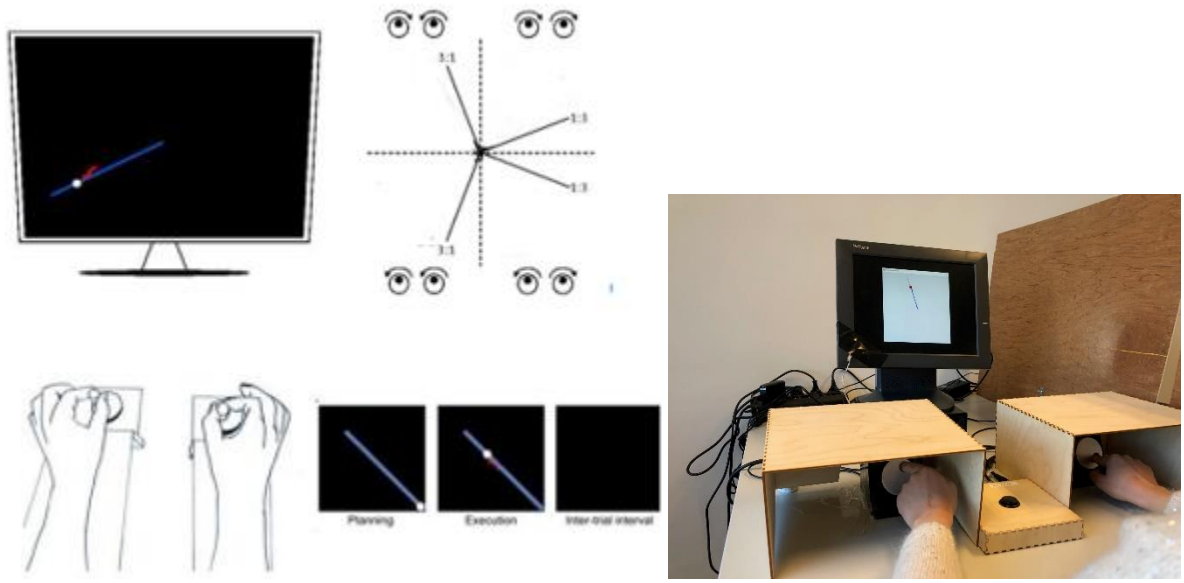

Fig3. *The bimanual tracking task. The experimental setup. Coordination patterns and frequency ratio. (Boisgontier, 2018)*

Protocol

At the beginning of the motor task, participants completed a practice session of 16 trials in order to understand the task and to familiarize with the task without stimulation. Following the practice session of five minutes, the stimulation-electrodes were placed, contact between the electrode and the skin was optimized with the TEN-20 paste. After this, the participants were exposed to one of the two or three possible stimulation conditions: in-phase tACS, anti-phase tACS or sham. This stimulation was applied on the right DLPFC and PPC for approximately 20 minutes, starting at the beginning of the bimanual task. In the sham condition, the electrodes were placed in an identical fashion as in real tACS. This study was a single blind study whereby the participants did not know whether or not they received real stimulation or sham stimulation. The researchers were aware whether the participants received and the statistics were also blinded. This study consisted of one experimental session. The total duration of this session was approximately 100 minutes.

The bimanual tracking task (BTT) was divided into four experimental blocks with stimulation applied, of which every block had a duration of five minutes, consisting of 36 trials. Each trial started by displaying the target line that needed to be followed on the screen in front of the participants. They got a preparatory period of two seconds to prepare themselves in what direction and at what speed to turn. After two seconds a sound signal indicated the start of the movement period of five seconds. Between two trials there was a rest period of three seconds. Concurrently, the dot moved over the line, and the participants were instructed to follow it as accurately as possible by rotating the dials. When the four blocks of trials were completed two more questionnaires were filled in. The first questionnaire assessed the possible subjective

sensations of the stimulation, like tingling or itching. The second questionnaire was about what type of stimulation they thought they had (tACS or sham). At the end of the session, one last block of the bimanual task was conducted of five minutes without stimulation. This retention block was intended as a reference value to measure learning and to find out what the after-effects were of the stimulation.

3.3. Data-analysis

For the analysis two different outcomes were measured to describe the quality of the BTT task: average trace deviation (ATrD) and average target deviation (ATaD). Where ATrD is a measurement of how much the line deviated from the illustrated line and where ATaD was considered based on how much the participants dot deviated from the given dot. To perform the statistics, for each block the average across trials was calculated.

Before the main analysis, the baseline performance level of the participants was compared. The used statistical tests are different for the YA and the OA. As the YA consisted of 31 people, a 1-sample t-test is used. On the other hand, the group of the OA is with less than 30 people (15 OA) and the data was not distributed normally, so the signed-rank sum test had to be used.

The purpose of the first two statistics was to find if there was any effect and what the effect was of the different stimulation forms in both groups separately (YA and OA). Thus, two analyses had to be done. On the one hand the analysis with the YA. A mixed model was used. The fixed effects were the different stimulation forms (in-phase, antiphase and sham) together with the stimulation block. The participants were used as a random effect. The ATrD and the ATaD were used as the dependent variable. On the other hand, there was the analysis with the OA. The same parameters were used, but in this group the stimulation form was either in-phase stimulation or antiphase stimulation.

A post hoc test (Tukey HSD) was done for the blocks to get a better view of the effect in both ATrD and ATaD in the OA and YA separately.

The goal of the third analysis was to investigate the difference between YA and OA. The analysis that was used was a mixed model. The fixed effects were the stimulation form (inphase or antiphase, because the sham stimulation was not used in the elderly group), the stimulation block (block one to block five) and the age. As a random effect the subject was used. ATrD and ATaD were used as the dependent variable. A post hoc test (Tukey) was used to get more details.

The next analysis that was done, was to look if here was any influence of the aftereffects (block 5, ret), to find out if there was a higher significant effect. The same analysis was done as for the third research question, but the parameter block was now block one to block four.

4. Results

Both groups individually (OA and YA) started with the same baseline before they performed the task with stimulation. Both the YA and OA started at the same baseline when looking at the within-group comparison, see table 1.

Table 1. *Analysis at baseline*

	N	P-value ATrD	P-value ATaD
Younger people	31	0.003	0.8669
Elderly people	15	0.6698	1.000

ATrD: Average Trace Deviation. *ATaD*: Average Target Deviation

A boxplot is used to get a first impression of the data for every research question, there was looked for possible outliers.

In all the boxplots, outliers were visible (marked as the black dots in the figures 5A and 5B).

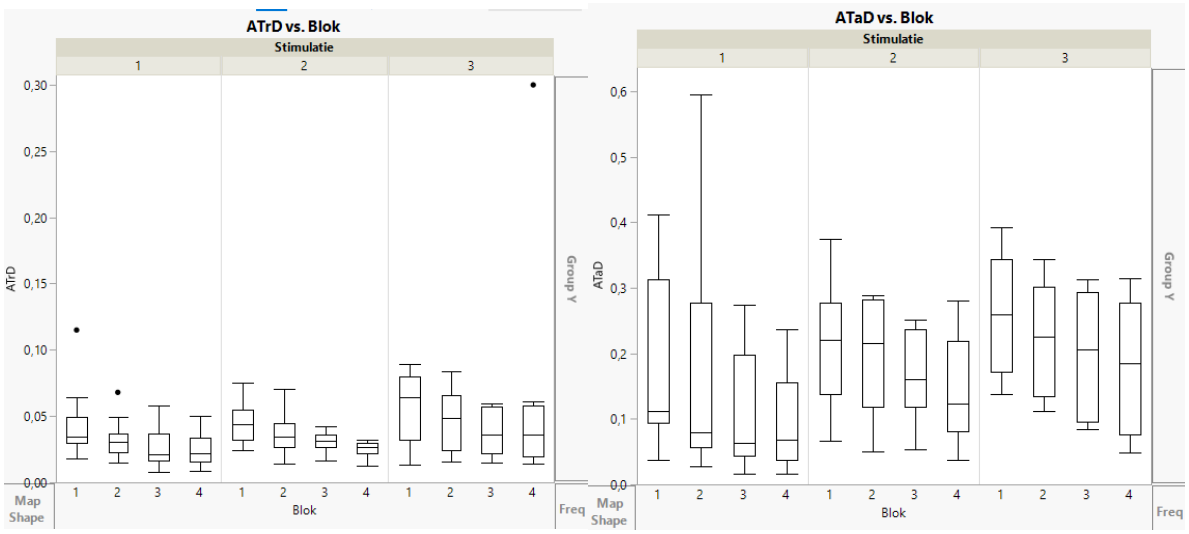

Figure 5A. *Research question one – effects of the different stimulation forms (YA: ATrD and ATaD). Stimulation forms: 1 = in-phase, 2 = antiphase, 3 = sham.*

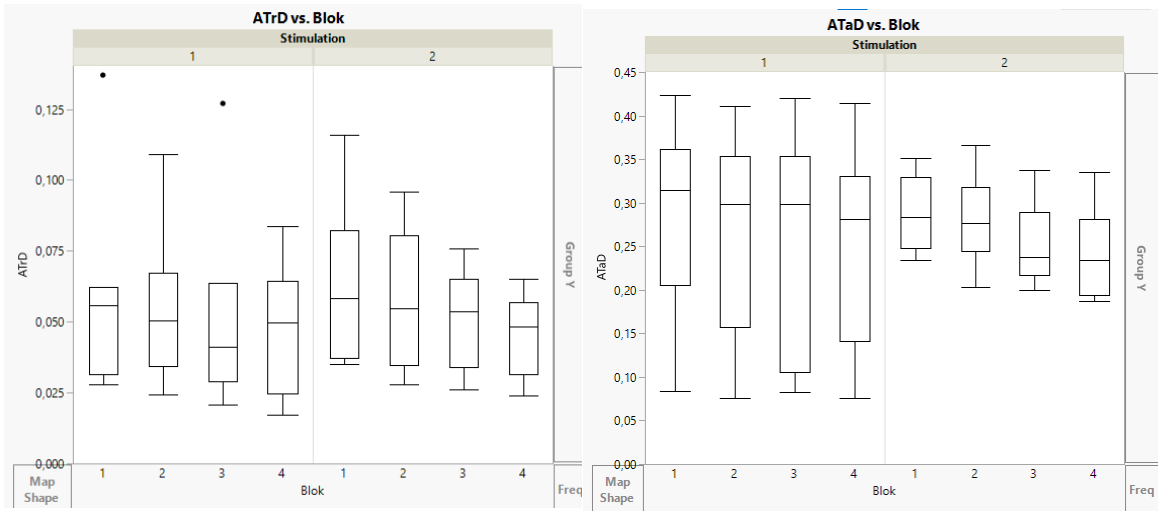

Figure 5B. *Research question one – effects of the different stimulation forms (OA: ATrD and ATaD). Stimulation forms: 1 = in-phase, 2 = antiphase.*

Research question one and two can be divided into two sub questions. On the one hand, looking at the YA whether there is an effect and what the effect is and on the other hand looking at the OA. In the YA there is no effect of stimulation form (p = 0.0776) (in-phase, antiphase or sham) and there is no effect of block (p = 0.0714) for the ATrD variable. For ATaD in the YA there is a significant effect of the factor block (p <0.0001), seen in table 2A. More specifically, there was a low significant effect between block 1 and 3 (p = 0.0478) for ATrD and there were 4 significant effects for ATaD: between block 1 and 3 (p <0.0001), between block 1 and 4 (p <0.0001), between block 2 and 3 (p = 0.0029) and between block 2 and 4 (p <0.0001).

In the OA there was a significant effect for block for ATrD (p = 0.0002). For ATaD there also was a significant effect for the factor block (p <0.0001), seen in table 2B. Significant effects were found for ATrD between block 1 and 3 (p = 0.0392), between block 1 and 4 (p = 0.0001) and between block 2 and 4 (p = 0.0177). ATaD showed significant effects between 1 and 3 (p = 0.0027), between 1 and 4 (p = 0.0002) and between 2 and 4 (p = 0.0091) (Appendix – 5. Statistical analysis; 5.2.2).

Table 2A. *Mixed model analysis younger adults*

	Stimulation				block	
	N In-phase	N Antiphase	N Sham	P-value	N	P-value
ATrD	12	11	8	0.0776	5	0.0714
ATaD				0.1930	5	<0.0001*
Ntotaal	31					

ATrD: Average Trace Deviation. *ATaD*: Average Target Deviation

Table 2B. *Mixed Model analysis older adults*

	Stimulation				block	
	N In-phase	N Antiphase	N Sham	P-value	N	P-value
ATrD	7	8	/	0.9649	5	0.0002*
ATaD				0.9249	5	<0.0001*
Ntotaal	15					

ATrD: Average Trace Deviation. *ATaD*: Average Target Deviation

Lastly, the research question is related to the effects between the two age groups associated with the different forms of stimulation. In relation to this question, a hypothesis was established whereby it is expected that the greatest effect will be seen in the OA and in in-phase stimulation. For the analysis across block one to five, the effect for age group is significant in both ATrD (p = 0.0005) and ATaD (p = 0.0009), where in the results of the analysis the effects will be greater among the YA than among the OA. The stimulation form was not found significant for both ATrD (p = 0.7363) and ATaD (p = 0.3191). The post hoc test (Tukey) showed more details here was a significant effect for ATrD between block 1 and 2 (p = 0.0036),

between 1 and 3 (p <0.0001), between 1 and 4 (p <0.0001), between 1 and 5 (p <0.0001), low significant effect between 2 and 3 (p = 0.0431), between 2 and 4 (p <0.0001), between 2 and 5 (p <0.0001) and between 3 and 5 (p = 0.0019). For ATaD the analyses showed a significant effect between block 1 and 3 (p <0.0001), between block 1 and 4 (p <0.0001), between block 1 and 5 (p <0.0001), between block 2 and 3 (p = 0.0015), between block 2 and 4 (p <0.0001), between block 2 and 5 (p <0.0001) and between block 3 and 5 (p = 0.0396) (figure 4A).

Table 3A. *block one to block five.*

	Stimulation				block		Age		
	N In-phase	N Antiphase	N Sham	P-value	N	P-waarde	Young	Old	P-value
ATrD	19	19	/	0.363	5	<0.0001*	23	15	0.0005*
ATaD				0.3191	5	<0.0001*			0.0009*
N total	38								

ATrD: Average Trace Deviation. *ATaD*: Average Target Deviation

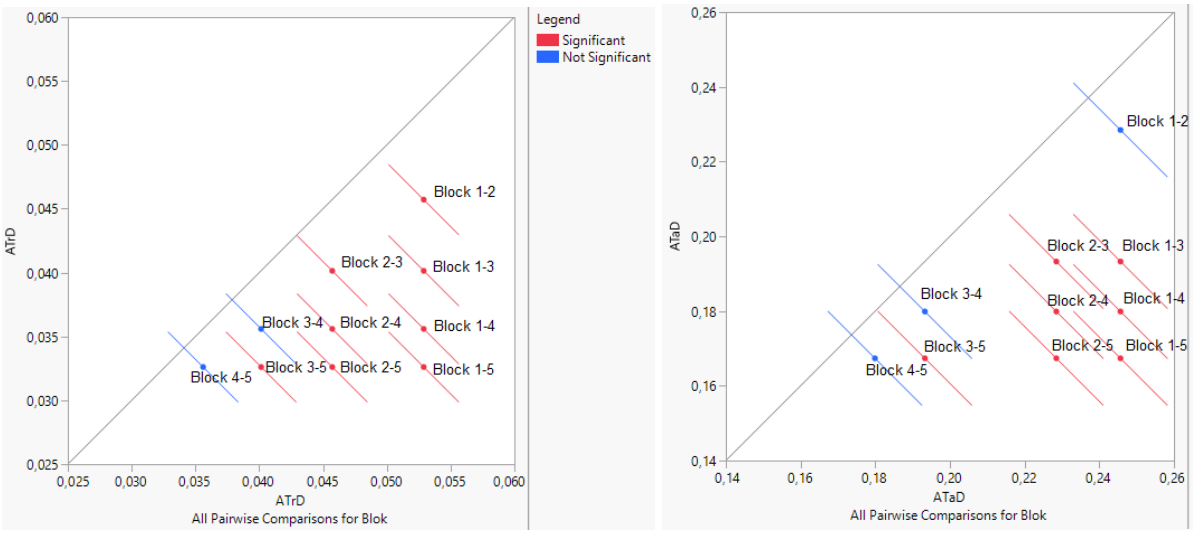

Figure 4A. *All pairwise comparisons Scatterplot block one to five.*

In the analysis without block 5 (without the retention block), the same factors were significant. For the variable block both in ATrD (p <0.0001) and ATaD (p <0.0001). Also in the variable age, there is a significant effect for ATrD (p = 0.0015) and ATaD (p = 0.0020) (table 3B). The effects of ATrD were significant between block 1 and 2 (p = 0.002), 1 and 3 (p <0.0001), 1 and 4 (p <0.0001), 2 and 3 (p = 0.0253) and 2 and 4 (p <0.0001). For ATaD the significant effects were found between block 1 and 3 (p <0.0001), 1 and 4 (p <0.0001), 2 and 3 (p = 0,001) and 2 and 4 (p <0.0001) (figure 4B).

Table 3B. *block one to four.*

	Stimulation				block		Age		
	N In-phase	N Antiphase	N Sham	P-waarde	N	P-waarde	Young	Old	P-waarde
ATrD	19	19	/	0.7923	4	<0.0001*	23	15	0.0015*
ATaD				0.3331	4	<0.0001*			0.002*
N total	38								

ATrD: Average Trace Deviation. *ATaD*: Average Target Deviation

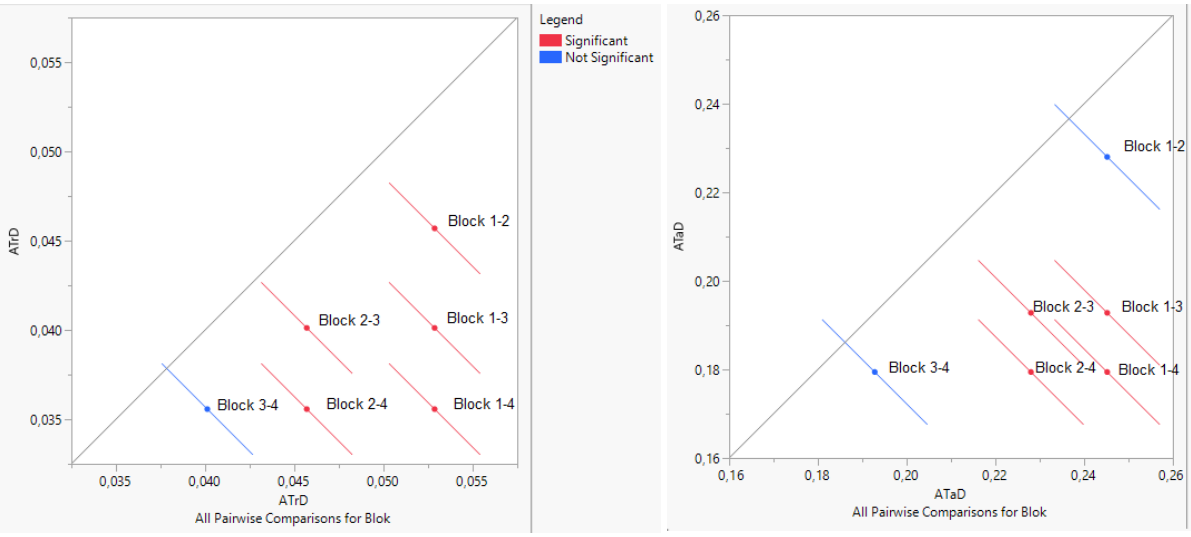

Figure 4B. *All pairwise comparisons Scatterplot block one to four*

5. Discussion

The purpose of this study was to examine the differences of tACS stimulation between older and younger adults and if the different stimulation types had a different effect on a bimanual task. As mentioned earlier those stimulations were in-phase, antiphase and sham.

To start, the performance at baseline was assessed to make possible statements about the analyses that were performed. In doing the statistical test, it was seen that within-group comparisons with the same age (OA or YA) the baseline was at the same level. This means a comparison can be made about the evolution in the performance of the task and of the effect of the stimulation.

Comparing the statistical results with the boxplots, in the different boxplots of the YA and OA separately the mean of ATrD and ATaD of the OA looks more stable compared to the YA. So it looks like they did not improve over time like the YA did. This is also seen in the statistical analysis when both age groups were compared to each other. The stimulation was not significantly different in any analysis. But looking at the boxplot of the YA, ATrD is at a lower level for in-phase and antiphase stimulation compared to sham stimulation. Also the decline appears faster in these two stimulation forms compared to sham stimulation. In both ATaD and ATrD in YA, in-phase stimulation reaches a lower level but it seems like anti-phase stimulation is still declining. For ATaD anti-phase stimulation has the biggest decline of all stimulation forms and in-phase stimulation has the lowest value in the YA. The boxplot of the OA is not that clear and corresponds to the statistical analysis.

In the boxplots where factor age is considered in the blocks one to five a comparison of the stimulation forms was done. ATrD declines more with antiphase stimulation seen in the boxplots, but this was not confirmed in the statistical analysis. From block one to four, the boxplots shows that antiphase stimulation has the biggest decline in ATrD and ATaD, but the effect is not found significant. With the boxplots there was seen that the baseline of the OA was at a lower level than the YA, as expected. This was already mentioned earlier. As we age, there are changes in the brain that cause the performance of motor tasks to decline (Larivière, et al., 2019).

For the first and second questions, we examined whether there was an effect of stimulation and where this effect had the greatest impact. It should be stated here that our hypothesis is incorrect. Where the expectation was made that there would be an effect of stimulation, with the greatest effect to be found at in-phase stimulation. This because in-phase uses waves that are synchronous to each other and are thought to couple the target structures (e.g., up-regulating functional cooperation, Polanía et al., 2012; Reinhart, Nguyen, 2019). Another reason for this way of thinking is because in-phase stimulation provides greater connectivity between brain parts compared to antiphase stimulation (Schwab, Misselhorn, Engel, 2019).

Looking at the results stimulation in the YA had no significant effect on the quality of the BTT. However, the task was done better over time, especially for ATaD. Thus, the quality of performance improved over time in both ATrD and ATaD. But no significant effect for stimulation form were found in the results. Since the improvements are not due to the stimulation form, they can possibly be explained by learning effects. When these effects were looked at in more detail, the most effects are found between blocks 1 and 3, 1 and 4. As well, more effects were found with ATaD than with ATrD. Where the reasoning was made that it is harder at the beginning of the task to follow the dot than following the line, so there is a greater opportunity for improvements. This means that overall, greater progress can be made with ATaD compared to ATrD.

For the third research question, the effect of stimulation and age were taken together. The effect of stimulation remains the same in this analysis as in the previous question. This makes it also necessary to reject this hypothesis. But for the variable age, a significant effect was found, with the significance referring to young people which was not according to our expectations. It was found that there was a greater improvement across the different blocks in the YA compared to the old people. This may be explained by the fact that OA learn a motor skill at a slower rate and that they did not show neural activation that overlapped with the early adaptation period (King, Fogel, Albouy, Doyon, 2013; Anguera et al.,2011).

In all of this, it is important to keep in mind that our data is not normally distributed and that variances are equal. To create a higher probability that H0 will be rejected on the right terms a large power is needed, which is related to sample size. In this current study the sample size is small for OA which makes that there is a smaller power. When this is small, the probability of a type 2 error will increase. Which is going to cause that H0 will be rejected because no effect was measured, when in reality it has an effect.

This study has some limitations, because of the covid-19 virus, the study design changed from a cross-over within-subject study to a single-session between-subject study. Consequently, there only was data of one stimulation form per participant. Where it was the intention to collect data of each participant in the three different stimulation types. Secondly, the group of the YA were twice the size of the OA. The YA were with 31 participants while the OA were with 15 participants. The group of the OA did not receive the sham stimulation, because of the lack of results of this third stimulation form the statistics were not performed as desired. Also, there is selection bias, the researchers had to collect participants, so a lot of researchers did ask friends to participate. Another limitation of this study was the fact that there were a lot of outliers in the database. To compensate, the same statistics were done to compare these two. After the second analysis without the outlier there were no differences in the outliers.

Future studies should aim to include more OA. Ultimately, OA are a highly interesting target group, from a therapeutical point-of-view. Also, the long-term effects should be investigated,

by doing different measurements over a certain time period. These long-term efficacy and different schedules need to be investigated to determine the real feasibility of tACS as an add-on home therapy on one hand, and to find out if there are lasting effects without repeated stimulations on the other hand. In this current study it was impossible, due to the covid-19 virus. This same recommendation on our memory. It was found that memory of the task happens over a longer time whether or not during sleep, which is needed motor adaptive storage (Brashers-Krug et al., 1996; Shadmehr and Brashers-Krug, 1997; Shadmehr and Holcomb, 1997, 1999; Krakauer et al., 2005). The final suggestion made regarding future studies is to target a different brain area, combined with another stimulation frequency. Stimulating the primary motor cortex (M1) may yield greater effects and may be more affected by the stimulation forms. Depending on this stimulated area, tACS will yield different effects. For example, Miyaguchi et al. (2018) has shown that anti-phase tACS over the bilateral M1, targeting gamma-band activity, improved motor performance in subjects with low performance by strengthening the network between these two stimulated cortices (Miyaguchi et al., 2018). For the adjustment of frequency bands, we look at the study of Giustiniani, Tarantino, Bonaventura, Smirni, Turriziani, Oliveri (2019). They found that stimulation in a low-gamma frequency (40 Hz) had effects on primary motor cortical reactivity. Also, the functions attention, perception and memory, learning and higher cognition were investigated (Tavakoli, Kyongsik, 2017). But to adjust brain regions and frequency, more research will be necessary.

Overall, we can conclude that the quality of the BTT task improved over time, this can be due to learning effect, regardless of age. On the other hand, YA have a better quality of the BTT than the OA. An effect of stimulation was not found. Clear statements cannot be made about the stimulation form. It seemed like tACS could improve the quality of the task, compared to sham but no significant effects were found. Differences between in-phase and antiphase stimulation were not found. Further studies with a larger population need to be done to investigate the effects of tACS.

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7. Appendix

1) Vragenlijst voor voorkeushand (Oldfield)

Vragenlijst voor voorkeurshand (Oldfield)

(vertaling)

Oldfield, R.C. (1971) The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia*, **9**(1), pp. 97113.

CODE: .....
TESTDATUM: ...../...../.....
SCORE: .....

INSTRUCTIES:

- Geef bij de onderstaande activiteiten weer welke hand u verkiest te gebruiken door een „+" te plaatsen in de passende kolom.
- Als de voorkeur voor die hand zo sterk is dat u nooit de andere hand zou gebruiken bij die taak, geef dit dan weer met een „++".
- Als u echt geen voorkeur hebt voor één van beide handen, plaats dan een „+" in beide kolommen.
- Voor sommige zijn beide handen nodig. Tussen haakjes staat dan aangegeven voor welke hand de voorkeur gevraagd is.
- Probeer alle vragen te beantwoorden, en laat enkel een vraag onbeantwoord als u echt geen ervaring hebt met de taak.

		links	rechts
1	**Schrijven**		
2	**Tekenen**		
3	**Werpen**		
4	**Knippen**		
5	**Tanden poetsen**		
6	**Mes (zonder vork)**		
7	**Lepel**		
8	**Bezem (bovenste hand)**		
9	**Een lucifer aansteken (hand die de lucifer vasthoudt)**		
10	**Een doos opendoen (hand die het deksel vastgrijpt)**		

Berekening van de lateraliteitsquotient: LQ= 100 * [(Som van "+" voor rechts) – (Som van "+" voor links)] / (Som van alle "+") Positief LQ: Rechtshandig; Negatief LQ: Linkshandig

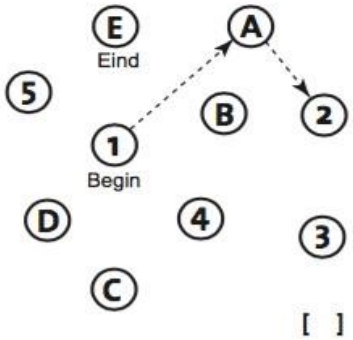
2) Montreal cognitive assessment (MoCA)

Nederlandse versie

MONTREAL COGNITIVE ASSESSMENT (MOCA)

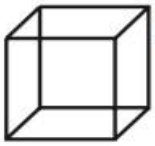
Geboortedatum: Code:
Jaren opleiding: Naam:
Geslacht: Datum:

VISUOSPATIEEL/EXECUTIEF — PUNTEN



[ ] [ ]

Kopieer de kubus

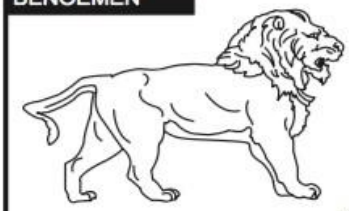


Teken een klok (tien over elf) (3 punten)

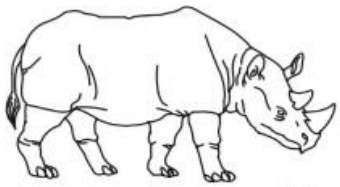
[ ] Omtrek [ ] Cijfers [ ] Wijzers

__/5

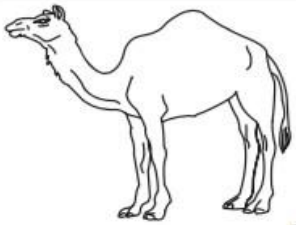
BENOEMEN



[ ]



[ ]



[ ]

__/3

GEHEUGEN — Lees de woorden op, proefpersoon moet ze nazeggen. Neem 2 maal af. Laat ze na 5 min. opnieuw opnoemen.

	GEZICHT	FLUWEEL	KERK	MADELIEF	ROOD
1e afname					
2e afname					

Geen punten

AANDACHT

Lees de rij cijfers op (1 cijfer/sec). Proefpersoon moet ze in dezelfde volgorde nazeggen [ ] **21854**
Proefpersoon moet ze in omgekeerde volgorde nazeggen [ ] **7 4 2** __/2

Lees de rij letters op. De proefpersoon moet bij iedere letter A met zijn hand op de tafel tikken. Geen punten bij ≥ 2 ft
[ ] **F B A C M N A A J K L B A F A K D E A A A J A M O F A A B** __/1

Serieel 7 aftrekken, beginnend bij 100 [ ] **93** [ ] **86** [ ] **79** [ ] **72** [ ] **65**
4 of 5 goed: **3 pt** 2 of 3 goed: **2 pt** 1 goed: **1 pt** 0 goed: **0 pt** __/3

TAAL

Zeg na: Ik weet alleen dat Jan vandaag geholpen zou worden. [ ]
De kat verstopte zich altijd onder de bank als er honden in de kamer waren. [ ] __/2

Fluency: Noem binnen één minuut zo veel mogelijk woorden die beginnen met de letter D [ ] (N ≥ 11 woorden) __/1

ABSTRACTIE

Overeenkomst tussen bijv. banaan en sinaasappel = fruit [ ] trein-fiets [ ] horloge-liniaal __/2

UITGESTELDE RECALL

	Woorden moeten herinnerd worden **zonder cue**	GEZICHT [ ]	FLUWEEL [ ]	KERK [ ]	MADELIEF [ ]	ROOD [ ]
Optioneel	Categoriecue					
	Meerkeuzecue					

Punten alleen voor recall zonder cue __/5

ORIËNTATIE

[ ]Datum [ ] Maand [ ] Jaar [ ] Dag [ ] Locatie [ ] Plaats __/6

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Normaal ≥ 26 / 30

TOTAAL __/30

Tel er 1 pt bij op indien ≤ 12 jr opleiding

3) TES screening questionnaire

	JA	NEEN
Heeft u metalen (uitgezonderd titanium) of elektronische implantaten in de hersenen/schedel (bv. splinters, fragmenten, clips, cochleair implantaat, diepe hersenstimulatie, etc.)? Indien ja, specifieer het type metaal en de locatie:		
Heeft u metalen of elektronische implantaten in een ander deel van uw lichaam (pacemaker, metalen fragmenten, etc.)? Indien ja, specifieer het apparaat en de locatie:		
Heeft u ooit chirurgische ingrepen gehad aan het hoofd of aan de ruggengraat? Indien ja, specifieer de locatie:		
Heeft u ooit een hoofdtrauma gehad waarna je het bewustzijn bent verloren?		
Heeft u huidproblemen zoals dermatitis, psoriasis, of eczeem? Indien ja, specifieer de locatie:		
Heeft u epilepsie of heeft u al stuiptrekkingen of een epileptisch insult gehad?		
Heeft u last van appelflauwtes of syncopes?		
Bent u zwanger of bestaat de kans dat u zwanger bent?		
Neemt u medicatie? Indien ja, specifieer:		
Bent u allergisch? Indien ja, specifieer:		
Heeft u in het verleden al eens transcraniële magnetische of elektrische neurostimulatie gehad? Indien ja, had u toen ergens last van? Specifieer:		

Een bevestigend antwoord op bovenstaande vragen is geen absolute contra-indicatie voor transcraniële neurostimulatie maar een herevaluatie van de risico's kan nodig zijn. Bij twijfel wordt er contact opgenomen met de arts-onderzoeker.

Code kandidaat (in te vullen door de onderzoeker): Handtekening en datum:

4) Vragenlijst stimulatie

Vragenlijst stimulatie

In te vullen door de onderzoeker:

Code kandidaat: Datum: Sessie: Onderzoek: Stimulatiecode: Elektrode: anode = .. x .. cm; cathode = .. x .. cm Eerste stimulatie (schrappen wat niet past)? Ja / nee #stimulaties voordien:

In te vullen door de kandidaat

Geef aan of u een van de onderstaande ongemakken heeft gevoeld tijdens de stimulatie, en vermeld de ernst van het ongemak via de volgende schaal:

- **Geen**: Ik heb het ongemak niet gevoeld tijdens de stimulatie
- **Mild**: Ik heb het ongemak slechts heel licht gevoeld tijdens de stimulatie
- **Gematigd**: Ik heb het ongemak gevoeld tijdens de stimulatie
- **Sterk**: Ik heb het ongemak zeer duidelijk gevoeld tijdens de stimulatie

Ongemakken gevoeld tijdens de stimulatie:				
	Geen	*Mild*	*Gematigd*	*Sterk*
Jeuk				
Pijn				
Branden				
Warmte				
Metaalsmaak				
Vermoeidheid				
Andere				

Specifieer Andere:

……

Wanneer begon u het ongemak te voelen?

Ongemakken gevoeld tijdens de stimulatie:				
	Geen	*In het begin*	*In het midden*	*Naar het einde toe*
Jeuk				
Pijn				
Branden				
Warmte				
Metaalsmaak				
Vermoeidheid				

Andere				

Hoe lang duurde het ongemak (meerdere opties mogelijk)?

Ongemakken gevoeld tijdens de stimulatie:					
	Geen	*Enkel in het begin*	*Gestopt in het midden*	*Gestopt op het einde*	*Gestopt na de stimulatie*
Jeuk					
Pijn					
Branden					
Warmte					
Metaalsmaak					
Vermoeidheid					
Andere					

In hoeverre heeft dit ongemak /hebben deze ongemakken uw algemene toestand beïnvloed?

☐ Helemaal niet □ Mild □ Gematigd □ Sterk

Locatie van het ongemak:

☐ Verspreid □Gelokaliseerd □Dicht bij de elektrode, ……
□Andere ……

Denkt u dat u actief gestimuleerd bent geweest of met de placebo stimulatie (sham)?

☐ Actief □Sham □Geen idee

AEs per elektrode:

……
……
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…….

Opmerkingen:

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…….

5) Statistical analysis

5.1 Checking baseline

To find out if the different participants started at the same level, an analysis was performed to compare the familiarization blocks. Here, a separate analysis was done for both young people and the elderly. The young people were with a group of more than 30 participants, which makes that a one sample T-test could be performed (Table 5.1). The average taken is the median of all outcomes. Because the elderly people were a smaller group (15), the singed-rank test had to be performed. The median was also taken as the estimated mean.

Table 5.1.1 – *One sample t-test and singed-rank sum from baseline*

	Younger adults (n = 31)		Older adults (n = 15)	
	ATrD	ATaD	ATrD	ATaD
Quantiles: 50%	0.056	0.313	0.0568	0.335
Test mean				
Hypothesized value	0.056	0.313	0.0568	0.335
Actual estimate	0.08456	0.31065	0.06266	0.33087
	T-test			**Signed-rank sum**
Test statistics	1.3096	-0.1690	7.5000	-0.5000
Prob > |t|	0.2003	0.8669	0.6698	1.000
Prob > t	0.1001	0.5666	0.3349	0.500
Prob < t	0.8999	0.4334	0.6651	0.500

5.2 Separate analysis of young and elderly adults

To answer research questions one (is there an effect of the stimulation on the quality of performance of the task?) and two (at what form of stimulation is the effect the greatest?), analyses of the 2 ages were conducted separately. A mixed model was performed, over the 4 experimental blocks. The model was simplified by taking out the interactions that were not significant. For the younger age group, a comparison was made with the three different forms of stimulation. For the elderly, two forms of stimulation were compared. Stimulation [1] represents the in-phase tACS stimulation and Stimulation [2] represents the antiphase tACS stimulation.

Table 5.2.1 – *A. Mixed Model younger adults*

	ATrD	ATaD
Fixed Effects Tests		
Source	**Prob > F**	**Prob > F**
Stimulation	0.0776	0.1930
Block	0.0714	<0.0001*

Table 5.2.1 – *B. Mixed Model older adults*

	ATrD	ATaD
Fixed Effects Tests		
Source	**Prob > F**	**Prob > F**
Stimulation	0.9649	0.9249
Block	0.0002*	<0.0001*

To find between which blocks there was a significant effect, a Tuckey Pairwise Comparison was done.

Table 5.2.2 – *A. All pairwise differences younger adults*

		ATrD	ATaD
Block	**-Block**	**Prob > |t|**	**Prob > |t|**
1	2	0.4870	0.1093
1	3	0.0478*	<0.0001*
1	4	0.2825	<0.0001*
2	3	0.6220	0.0029*
2	4	0.9827	<0.0001*
3	4	0.8349	0.4243

Table 5.2.2 – *B. All pairwise differences older adults*

		ATrD	ATaD
Block	**-Block**	**Prob > |t|**	**Prob > |t|**
1	2	0.3414	0.5454
1	3	0.0392*	0.0027*
1	4	0.0001*	0.0002*
2	3	0.6993	0.0859
2	4	0.0177*	0.0091*
3	4	0.2015	0.8008

5.3 Analysis with younger adults and older adults together

For the last research question the goal was to find out if there are any differences between younger and elderly people. The analysis that was used was a mixed model. All the data was put together in one database. The fixed effects were the two stimulation forms (inphase and antiphase), the stimulation block (block one to block five) and the two age groups. As a random effect subject was used. These were all imported as categorical data. ATrD and ATaD were used as the dependent variable. With this data, another Mixed Model analysis was done omitting block five. So, the analysis was done over the various blocks one to four.

Table 5.3.1 – *A. Block one to five*

	ATrD	ATaD
Fixed Effects Tests		
Source	**Prob > F**	**Prob > F**
Age	0.0005*	0.0009*
Stimulation	0.7363	0.3191
Block	<0.0001*	<0.0001*

Table 5.3.1 – *B. Block one to four*

	ATrD	ATaD
Fixed Effects Tests		
Source	**Prob > F**	**Prob > F**
Age	0.0015*	0.0020*
Stimulation	0.7923	0.3331
Block	<0.0001*	<0.0001*

To find out between which blocks there was a significant effect, a Tuckey Pairwise Comparison was done.

Table 5.3.2 – *A. All pairwise differences block one to five*

		ATrD	ATaD
Block	**-Block**	**Prob > |t|**	**Prob > |t|**
1	2	0.0036*	0.3267
1	3	<0.0001*	<0.0001*
1	4	<0.0001*	<0.0001*
1	5	<0.0001*	<0.0001*
2	3	0.0431*	0.0015*
2	4	<0.0001*	<0.0001*
2	5	<0.0001*	<0.0001*
3	4	0.1515	0.5826
3	5	0.0019*	0.0396*
4	5	0.5600	0.6429

Table 5.3.2 – *B. All pairwise differences block one to four*

		ATrD	ATaD
Block	**-Block**	**Prob > |t|**	**Prob > |t|**
1	2	0.0020*	0.2341
1	3	<0.0001*	<0.0001*
1	4	<0.0001*	<0.0001*
2	3	0.0253*	0.0010*
2	4	<0.0001*	<0.0001*
3	4	0.0959	0.4540

5.4 boxplots

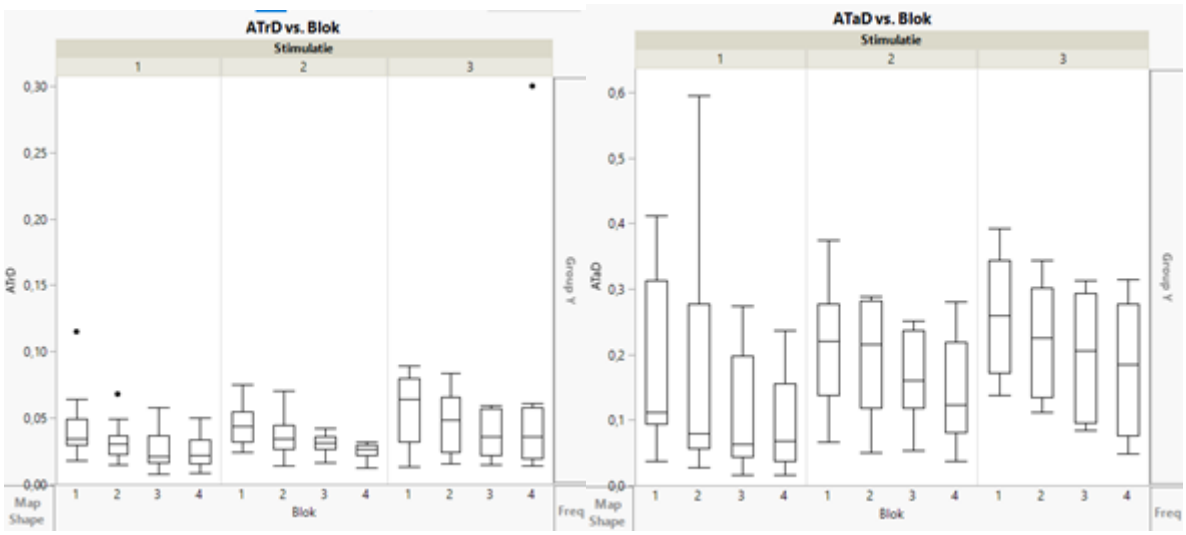

Figure 5.4 - A. *research question 1+2 – YA ATrD + ATaD. Stimulation forms: 1 = in-phase, 2 = antiphase, 3 = sham.*

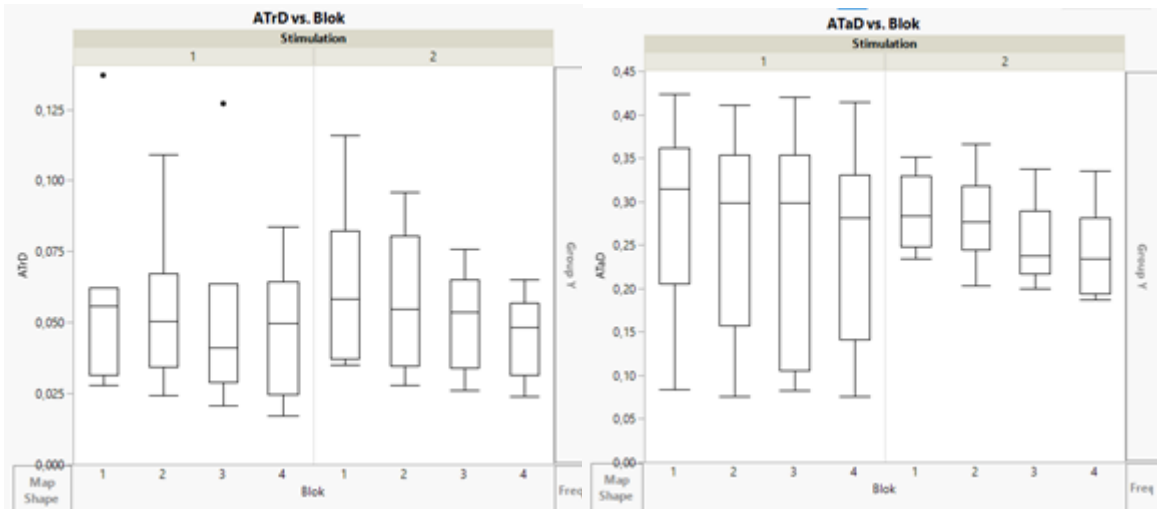

Figure 5.4 - *B. research question 2 – OA ATrD + ATaD. Stimulation forms: 1 = in-phase, 2 = antiphase.*

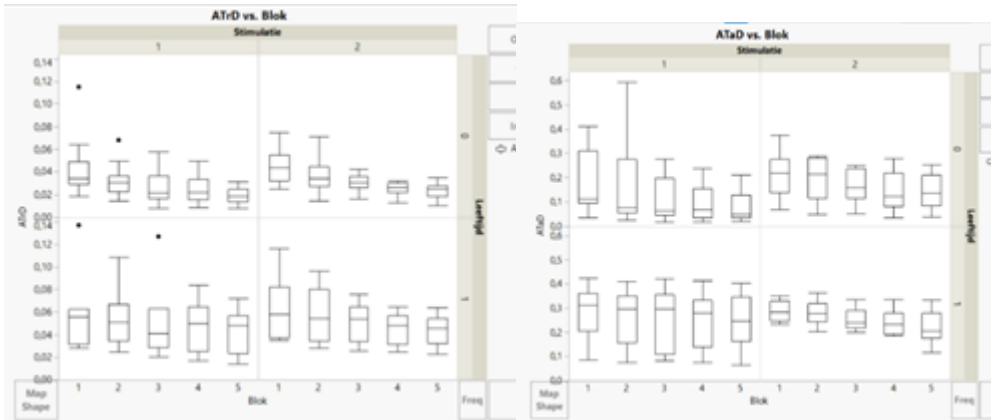

Figure 5.4 - *C. research question 3a – ATrD + ATaD.Stim:ulation forms: 1 = in-phase, 2 = antiphase, 3 = sham.*

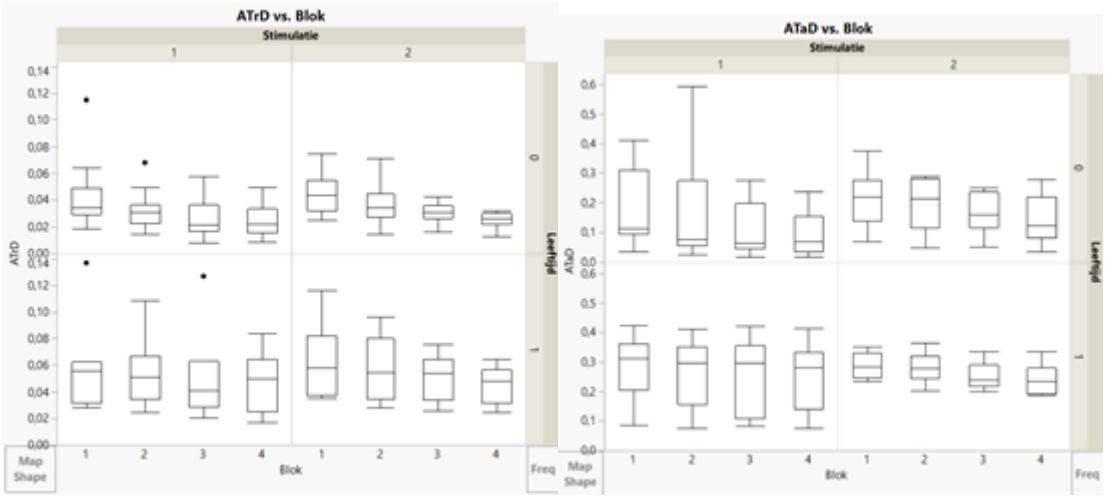

Figure 5.4 - *D. research question 3b – ATrD + ATaD. Stimulation forms: 1 = in-phase, 2 = antiphase.*

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KNOWLEDGE IN ACTION

INVENTARISATIEFORMULIER WETENSCHAPPELIJKE STAGE DEEL 2

DATUM	INHOUD OVERLEG	HANDTEKENINGEN
24/09/'20	Algemeen overleg + Praktische afspraken	Promotor: Copromotor/Begeleider: Student(e): Student(e):
28/10/'20	Uitleg onderwerp MP 2	Promotor: Copromotor/Begeleider: Student(e): Student(e):
28/11/'20	Feedback inleiding + methode	Promotor: Copromotor/Begeleider: Student(e): Student(e):
05/12/'20	Feedback inleiding + methode + Uitleg over vragenlijsten	Promotor: Copromotor/Begeleider: Student(e): Student(e):
11/02/'21	Informatie proefpersonen	Promotor: Copromotor/Begeleider: Student(e): Student(e):
01/03/'21	Uitleg statistiek	Promotor: Copromotor/Begeleider: Student(e): Student(e):
26/03/'21	Online meeting Feedback statistiek	Promotor: Copromotor/Begeleider: Student(e): Student(e):
26/04/'21	Feedback statistiek + discussie	Promotor: Copromotor/Begeleider: Student(e): Student(e):
27/05/'21	Finale versie feedback	Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):

In te vullen door de promotor(en) en eventuele copromotor aan het einde van MP2:

Naam Student(e): Myrthe Lousbergh en Tine Louwet **Datum:** 03/06/2021

Titel Masterproef: .....

1) Geef aan in hoeverre de student(e) onderstaande competenties zelfstandig uitvoerde:
   - NVT: De student(e) leverde hierin geen bijdrage, aangezien hij/zij in een reeds lopende studie meewerkte.
   - 1: De student(e) was niet zelfstandig en sterk afhankelijk van medestudent(e) of promotor en teamleden bij de uitwerking en uitvoering.
   - 2: De student(e) had veel hulp en ondersteuning nodig bij de uitwerking en uitvoering.
   - 3: De student(e) was redelijk zelfstandig bij de uitwerking en uitvoering
   - 4: De student(e) had weinig tot geringe hulp nodig bij de uitwerking en uitvoering.
   - 5: De student(e) werkte zeer zelfstandig en had slechts zeer sporadisch hulp en bijsturing nodig van de promotor of zijn team bij de uitwerking en uitvoering.

Competenties	NVT	1	2	3	4	5
Opstelling onderzoeksvraag	X	O	O	O	O	O
Methodologische uitwerking	X	O	O	O	O	O
Data acquisitie	O	O	O	O	X	O
Data management	O	O	O	O	X	O
Dataverwerking/Statistiek	O	O	O	O	X	O
Rapportage	O	O	O	O	X	O

2) Niet-bindend advies: Student(e) krijgt toelating/geen toelating (schrappen wat niet past) om bovenvermelde Wetenschappelijke stage/masterproef deel 2 te verdedigen in bovenvermelde periode. Deze eventuele toelating houdt geen garantie in dat de student geslaagd is voor dit opleidingsonderdeel.

3) Deze wetenschappelijke stage/masterproef deel 2 mag wel/niet (schrappen wat niet past) openbaar verdedigd worden.

4) Deze wetenschappelijke stage/masterproef deel 2 mag wel/niet (schrappen wat niet past) opgenomen worden in de bibliotheek en docserver van de UHasselt.

Datum en handtekening Student(e)	Datum en handtekening promotor(en)	Datum en handtekening Co-promotor(en)
2/06/2021	Raf MEESEN aan mij Beste Myrthe, Het antwoord op deze mail telt als handtekening voor U en Tine AKKOORD met de gemaakte inventarisatie, voor de competenties mag je bij de eerste twee NVT aankruisen, de andere 4 Mvg Op wo 2 jun. 2021 om 17:41 schreef Myrthe Lousbergh <myrthe.lousbergh@student.uhasselt.be>: ••• -- **Professor Raf Meesen** Professor, Neuroplasticity and Movement Control Head, Neurologic Rehabilitation research group Chairman, Rehabilitation Sciences and Physiotherapy Master program Vice-Director,Doctoral School Health and Life Sciences	