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# Effects of Transcranial Direct Current Stimulation of the Cerebellum (ctDCS) Associated with Cognitive Training in the Working Memory on Healthy Elderly

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***Abstract*—** *The present research presents a study with the intention of advancing the knowledge of the repercussions of the cerebellum stimulations. The study investigated the acute and cumulative effects of transcranial cerebellum current (ctDCS) stimulation associated with cognitive training for working memory in healthy elderly. A total of 30 volunteers, aged 60 to 72 years, underwent five sessions consisting of the application of the following protocols on the entire cerebellum hemisphere: the Experimental Group (15 participants) received an anodic electric current (anodic ctDCS) and the Control Group (15 participants) received a sham current (simulated ctDCS), both of whom underwent cognitive training while receiving transcranial anodyne cerebellar current or sham (online) stimulation. Participants' performances were measured through specific neuropsychological tests to assess working memory (Digit Span test in direct and indirect order and Letter-Number Sequencing test). After a week and three months of the last stimulation session, the participants performed the neuropsychological tests again to check for possible remnants of the intervention (follow-up). The results suggest that there was no difference between the performance of Experimental Group (anodic ctDCS) and Control Group (sham ctDCS) in different neuropsychological tests, regardless of the time of application ($p>0,05$). While the anodic ctDCS improved the performance of the Experimental Group in the intra-group analysis Digit Span test in direct order when compared to baseline and the follow-up three-month ($p<0,05$).*

***Keywords*— aging, cerebellum, cognitive training, transcranial direct current stimulation.**

## I. INTRODUCTION

In recent years, with the increase in research on the cerebellum, its circuits and functions (ITO, 2012), evidenced that its functions were not only related in the acquisition of motor skills, but also related in the execution of cognitive functions, emotional processing and behavior (BALDAÇARA et al., 2011).

The cerebro-cerebellum is involved with various regions of the cerebral cortex, in which its main entry involves the contralateral cerebral cortex. Their efferences are transmitted through the dentate nucleus that protrude into the cortex of prefrontal association, for example, involved in working memory (MARTIN, 2013).

In the process of aging, there are some changes in the cerebellum, such as a reduction in the volume, in the

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white matter (HOOGENDAMA et al., 2012; KOPPELMANS et al., 2015) and in the quantity of cells called Purkinje (ANDERSEN et al., 2003; WOODRUFF -PAK et al., 2010; ZHANG; ZHU; HUA, 2010).

Non-invasive brain stimulation techniques applied to the cerebellum have been used to understand the cerebellum during cognitive behaviors as well as to modulate cerebellum functions (GRIMALDI et al., 2016). Among the techniques, one of the most used is transcranial direct current stimulation (ctDCS) (GRIMALDI et al., 2014).

The ctDCS is a technique that uses continuous and low intensity electric current, capable of altering the excitability in the stimulated region and may induce the increase or decrease of excitability, depending on the polarity used. It is a non-invasive method, safe, painless, easy to apply and with few adverse effects (CRETAZ, 2017; MONTE-SILVA; BAPTISTA; BALTAR, 2017).

The ctDCS is also an interesting adjuvant tool in the treatment of several diseases of neurological, psychiatric and motor conditions (STAGG; NITSCHE, 2011), and can be used in conjunction with other cognitive techniques in the treatment of degenerative processes of dementia, cognitive training (SILVIA et al., 2017).

Cognitive training through specific cognitive activities aims at preserving or enhancing an individual's intellectual abilities in order to produce improvements in the performance of everyday tasks (NUNES, 2017).

Thus, this research aimed to investigate the effects of transcranial cerebellum current stimulation, associated with cognitive training of working memory in healthy elderly. Understanding these effects in healthy individuals helps to understand the physiology of the cerebellum in its typical state and thus to be able to develop prevention strategies and alternative therapeutic techniques for the rehabilitation of individuals with cognitive impairments.

## II. MATERIALS AND METHODS

The study consisted of 30 right-handed elderly volunteers aged 60 to 72 years (mean ≅ 66.3), 25 female and 5 male, recruited from the research group in Exercise, Nutrition and Central Nervous System (ENCNS) of the Department of Physical Education of the Federal University of Pernambuco (UFPE).

Design Research:

The TCT Stimulator (TCT Research Limited) was connected to a pair of silicon-carbon electrodes (35cm²) embedded in saline solution (NaCl 0.9%), the active electrode was centered especially the cerebellum in the midline 2 cm below the inion and 1 cm posterior to the mastoid process, while the reference electrode was positioned in the right deltoid muscle (FERRUCCI et al., 2013).

The participants received anodic stimulation with current intensity of 2mA and duration of 20 minutes (POPE; MIAL, 2012). To ensure safety, a current density of 0.028 mA / cm² was applied, since this value is below the threshold for damage (NITSCHE et al., 2003).

For the sham stimulation, the same protocol was used for the anodic stimulation, however, the electric current was applied with duration of 30 seconds which is not enough to cause a modulation (NITSCHE et al., 2008).

The realization of the cognitive training occurred individually and simultaneously to the transcranial stimulation by direct current. The training consisted of unimodal intervention focusing on the ability of working memory to verify its relation with the cerebellum.

The cognitive training was composed of five sessions (CARVALHO; NERI; YASSUDA, 2010; LIMA-SILVA et al., 2010; ARAMAKI; YASSUDA, 2011) with duration of one week. It should be noted that for each session a cognitive task was carried out that diversified between the "computer" model and "pencil and paper", in order to stimulate the intervention.

For the construction of the tasks, a gradual gradation of difficulty levels (easy, medium and difficult) was developed in order to increase motivation for adherence to training. (GOLINO, FLORES-MENDOZA, 2016). The materials used in the activities, including the records and instruction sheets were developed by the researchers, based on the literature.

**Cognitive Tasks:**

Cognitive task Visual N-Back: during the *Visual N-back Task*, images of animals were presented to participants at a distance of 60 centimeters from the computer screen. The volunteer's task was to judge whether the image that appeared at the time was similar to or different from the previous (1-back) image. To record the responses, two buttons were placed below the image shown, where the red corresponded that the current image was different from the previous one and the green image was the same as before. Participants were instructed to press one of the buttons on the computer screen with the mouse and a response time was not established.

Task Word List: This task was to present 4 word lists (50 words each list) of different categories (food, object, professions, hobbies / games) through slides. Each word was displayed on the computer screen for 2.4 seconds, totaling a time of 2 minutes for each list. The task of the elderly person was to read aloud the words in the list and,

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at the end of each one, to write on the answer sheet all the words that could be remembered in the time of 3 minutes.

Face Recognition Task: the task was to present a set of black and white frontal face images of men and women, taken from the Pictures of Facial Affect (POFA), Picture Bank developed by psychologist Paul Ekman (1997). The pictures presented facial expressions related to the six basic emotions (joy, sadness, disgust, fear, surprise and anger). Participants were instructed that the image of a face (target image) would be projected onto the computer screen. Then the image disappeared and a set of faces (image-option) was presented, in which the participant should identify which of these was the previously presented image (target image).

Genius Task: At the beginning of the activity, participants were given four red, blue, green and yellow circular tokens and a white, portable holder.

They were then instructed that a sequence of these colors would be displayed on the computer screen for 5 seconds, in which they should watch carefully so that after completion of the projection he tried to reproduce the sequence on the white medium, as he could remember.

Figure Arrangement Task: participants received the disordered WAIS-III Figure Arrangement test cards with pictures representing snippets of a story. The volunteer was instructed to order them by following a correct order of events. In all, there were 11 stories (items), in which they were counted and organized within pre-determined test times.

**Experimental Procedure:**

The volunteers initially answered a Sociodemographic Questionnaire, MoCa Cognitive Screening Test and the Geriatric Depression Scale (GDS-15), which served as eligibility criteria. After the screening, a randomization was performed, in which the participants were randomly divided into two groups, 15 for the Experimental Group, and 15 for the Control Group.

Participants were submitted to five sessions followed by cerebellar tDCS. In these sessions, the volunteers were individually submitted, for 20 minutes, to anodic stimulation for the Experimental Group and sham (fictive) for the Control Group. The two groups performed cognitive training during anodic tDCS or sham (online) stimulation depending on the group to which they were inserted.

The cognitive training was composed of five cognitive tasks, in which they were aimed at stimulating working memory. The experimental procedure will be detailed below.

• First session, the volunteers performed the tests of the digits and sequence of numbers and letters of the WAIS-III Scale Serving Baseline-T1 for the search (offline). Then the cerebellar ETCC intervention was performed with the N-back Task. After five minutes of the end of the stimulation, the Digit Tests and Sequence of Numbers and Letters of the WAIS-III Scale (T2) were reapplied. The objective was to ascertain the immediate effect of the stimulation compared to the performance of the participants in the initial tests (baseline).

• Second session, the volunteer performed the task of "word list" during the cerebellar anodic tDCS or sham.

• Third session, the task of "face recognition" was performed during cerebellar anodic tDCS or sham.

• Fourth session, the "Genius" Task was performed during the cerebellar anodic tDCS or sham.

• Fifth session, the cognitive task of "storytelling" was performed during the cerebellar anodic tDCS or sham.

After five minutes of the end of the stimulation, the tests of the digits and sequence of number and letters were applied again in order to verify cumulative effects (T3). After a week and three months of the last stimulation session, the follow-up was performed by reapplying the tests of the digits and sequence of number and letters (T4 and T5) in order to ascertain the remaining effects of the stimulation in the participants

**Data Analysis:**

There were 30 participants, but there was a loss of participants in the follow-up of one week and 1 in the follow-up of 3 months in the Experimental Group and in the Control Group. Thus, due to the losses during these moments of the study, the principle of intention-to-treat analysis was used.

The GLM test was used for repeated measurements to detect differences between Time and the effect between Time x Group on the dependent variables (direct-order digits, inverse order and sequence test of letters and numbers), we observed the criteria of normality from the Shapiro-Wilk and sphericity from the Mauchly Test, for the variables that did not present normality was used as a criterion of correction the standardization in Z score, when the sphericity was not detected, it was used the Greenhouse-Geisser Correction Criterion. The level of significance was set at 0.05.

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## III. RESULTS AND DISCUSSION

Thirty healthy elderly people participated in the research.

Data analysis is presented in the order of application of the neuropsychological instruments in the time function- T1 (baseline), T2 (second evaluation), T3 (third evaluation), T4 (follow-up one week) and T5 of three months) - for the two groups - Experimental (anodic ETCCc) and Control (ETCCc sham).

Based on the GLM test of repeated measures, it was observed that there is an interaction effect between Time and Group for the test of the digits in the direct order (F (3.04, 85.13) = 2.57, p = 0.04, eta square = 0.084 ).

The posthoc analysis (Bonferroni) of the interaction between time and group, showed that there is difference in the values of the tests in the direct order within the experimental group between time 1 and time 5 (p <0.05), however the interaction between Time and Group showed that there was no difference in the test values in the direct order within the Control Group (p> 0.05) between the five times

Regarding the results of the test of digits in the reverse order, GLM analysis showed that there is no effect on the interaction between Time and Group in both the intra-group analysis of the Experimental Group and that of the Control Group.

GLM revealed that there was no interaction effect between Time and Group for the sequence number and letters test in the intra-group analysis in both groups (p> 0.05).

In the comparison of the means of each subtest (direct order, inverse order and sequence of numbers and letters) between the Experimental and Control groups for all application times (T1, T2, T3, T4 and T5) there was no significant difference between the means of the groups (p> 0.05).

*Table 1 Mean performance among Experimental and Control groups in neuropsychological tests.*

| | TEST GROUP | MEAN | p |
|---|---|---|---|
| DDO | EXPERIMENTAL | 9,704 | 0,934 |
| | CONTROL | 9,762 | |
| ROD | EXPERIMENTAL | 4,007 | 0,395 |
| | CONTROL | 4,54 | |
| SNL | EXPERIMENTAL | 6,633 | 0,532 |
| | CONTROL | 6,167 | |

Subtitles: DDO: Digits of direct order; ROD: Reverse order digits; SNL: Sequence of numbers and letters. P * <0.05.

Concerning adverse effects, the participants reported sensations of pruritus, tingling, burning (mild), difficulty concentrating, drowsiness, redness. In addition to two participants who obtained a small first degree burn below the electrode in the right arm and metallic taste in the mouth in the anodic stimulation.

## IV. CONCLUSION

The results of this research showed that there was no significant difference between the group receiving anodic CTCC and the group receiving CTCC sham in the working memory tests. These findings confirm the idea that the concept of polarity-dependent is not well diffused for transcranial DC stimulation in the cerebellum, since in the literature there is no consensus on the types of stimulation responses (anodic, cathodic and sham) work memory.

There is evidence that cathodal stimulation may have a facilitating effect on the performance of participants in arithmetic tasks when compared to anodic and sham stimuli that do not show significant differences (POPE; MIAL, 2012).

On the other hand, studies have observed that anodic and cathodic stimulation on the cerebellum can impair the performance of participants in a task of remembering numbers (FERRUCCI et al., 2008), as well as differences between the three types of stimulation (anodic, cathodic and sham) in the results of the N-Back task (VAN WESSEL et al., 2016), suggesting that the effects of cerebellar CTEF may vary according to the tasks applied.

There was a difference in the results of the volunteers in the three tests for working memory, which may be related to the complexity of the task. The direct-order digit test requires a more direct relationship with the phonological loop, while reverse order and sequence of numbers and letters also requires the participation of the central executive system.

It is seen that the effects of cathodic and anodic stimulation on the cerebellum are not fully elucidated, a fact that may be linked by technical and experimental questions and the complexity of the cerebellum structure and its various connections with motor and / or cognitive activities during the protocol may to influence the effects of CTEF (Horvath and Carter, Forte, 2014). In addition, physiological and functional changes in the cerebellum relative to the aging process itself may influence the effects of cerebellar anodic ECCT.

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Regarding the specific training for working memory considering each group, the results of the means between the Experimental and Control group and the intra-group analysis of the Control Group did not present significant differences, suggesting that there were no transfer effects.

In relation to the adverse effects, it is seen that some studies even presenting protocols considered safe have reported burns after CTEC (WANG et al., 2015; WOODS et al., 2016; MELO, 2016). Other symptoms, such as metallic taste in the mouth, although not common, have also been reported in studies using transcranial direct current stimulation (FERRUCCI; CORTESE; PRIORI, 2015; MELO, 2016).

In conclusion, the limited number of studies that approach this methodology and the elderly population makes this project present an innovative character and thus contributes to the construction of new evidences and protocols for the investigation of cerebellar stimulation and cognitive training in order to improve the quality of life of the elderly population.

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