

ACUTE EFFECTS OF TRANSCRANIAL DIRECT CURRENT STIMULATION (tDCS) COMBINED WITH AEROBIC EXERCISE IN TREATING FOOD COMPULSION: A RANDOMIZED CONTROLLED TRIAL

Milena Artifon¹, Gabriel Mayer Tossi¹, Nathália Griebler¹, Pedro Schestatsky¹, Rodrigo Leal¹
Samuel Munhoz¹, Lucas Beraldo¹, Lauren Naomi Adachi¹, Caroline Pietta-Dias¹

ABSTRACT

Purpose: To investigate whether one session of transcranial direct current (tDCS) stimulation alone or combined with aerobic exercise (AE) could reduce food consumption and the perception of hunger and satiety in patients with binge eating disorder. **Materials and Methods:** Adult individuals with BED were recruited in a randomized, controlled, double-blind study. Participants received one session (1) active tDCS, (2) placebo and AE tDCS or (3) active tDCS and AE. tDCS was applied at 2mA / 20 min, with the anode over the right dorsolateral prefrontal cortex and the cathode over the contralateral supraorbital region. The AE was performed on a treadmill after tDCS, with initial warm-up and intensity of 60-65% of HRmax, repeating the evaluations at the end. Primary outcomes included measures of food intake and perceptions of hunger, satiety and desire. **Results:** The tDCS group had lower values of lean mass and triglycerides compared to the other groups. However, in relation to food intake, hunger, satiety throughout the day, and uncontrollable desire to eat, tDCS alone or combined were equally effective. **Conclusions:** tDCS alone or combined with AE improved clinical outcomes in patients with BED. To our knowledge, to date, this is the first study showing that the association of tDCS with aerobic exercise to relieve symptoms of patients with BE. **Test record:** ReBEC identifier RBR-3d8fd2.

Key words: Transcranial direct current stimulation. tDCS. Exercise. Binge eating.

1 - Exercise Research Laboratory, School of Physical Education, Physiotherapy and Dance, Federal University of Rio Grande do Sul, Porto Alegre, Brazil.

RESUMO

Efeitos agudos da estimulação transcraniana por corrente contínua (etcc) combinada com exercício aeróbico no tratamento da compulsão alimentar: um ensaio randomizado controlado

Objetivo: Investigar se uma sessão de estimulação transcraniana por corrente contínua (ETCC) isolada ou combinada com exercício aeróbico (EA) poderia reduzir o consumo alimentar e a percepção de fome e saciedade em pacientes com transtorno da compulsão alimentar periódica (TCAP). **Materiais e Métodos:** Indivíduos adultos com TCAP foram recrutados em um estudo randomizado, controlado e duplo-cego. Os participantes receberam uma sessão (1) tDCS ativo, (2) placebo e EA tDCS ou (3) tDCS ativo e EA. A ETCC foi aplicada a 2mA/20 min, com o ânodo sobre o córtex pré-frontal dorsolateral direito e o cátodo sobre a região supraorbitária contralateral. O EA foi realizado em esteira após ETCC, com aquecimento inicial e intensidade de 60-65% da FCmax, repetindo as avaliações ao final. Os resultados primários incluíram medidas de ingestão de alimentos e percepções de fome, saciedade e desejo. **Resultados:** O grupo ETCC apresentou valores menores de massa magra e triglicerídeos em relação aos demais grupos. No entanto, em relação à ingestão alimentar, fome, saciedade ao longo do dia e desejo incontrolável de comer, a ETCC isolada ou combinada foram igualmente eficazes. **Conclusões:** ETCC sozinho ou combinado com EA melhorou os resultados clínicos em pacientes com TCAP. Ao nosso conhecimento, até o momento, este é o primeiro estudo mostrando que a associação de tDCS com exercícios aeróbicos para aliviar os sintomas de pacientes com EB. **Registro de teste:** identificador ReBEC RBR-3d8fd2.

Palavras-chave: Estimulação transcraniana por corrente contínua. tDCS. Exercício. Compulsão alimentar.

E-mail author:
milena.artifon@gmail.com

INTRODUCTION

Binge eating, that is, the ingestion of a large amount of food, as well as inappropriate eating habits and physical inactivity are among the main causes related to excessive body weight increase and chronic diseases associated with lifestyle (Magno et al., 2014; Relton et al., 2014).

Recently defined, Periodic Compulsive Eating Disorder (BED) is a diagnostic category usually associated with psychopathology and being overweight, which can lead to obesity (Magno et al., 2014; Relton et al., 2014).

Evidence-based treatments for controlling excess weight currently available are mainly lifestyle interventions, pharmacotherapy, and bariatric surgery (Brownley et al., 2016).

Lifestyle interventions are the first option for weight loss, given their low cost and minimal risk of adverse effects and complications. Bariatric surgery is often recommended according to strict treatment criteria for patients who do not respond sufficiently to lifestyle therapy and / or pharmacotherapy (Brownley et al., 2016).

In this context, tDCS and aerobic exercises are well-tolerated, safe and non-invasive approaches that would act as a complementary treatment to lifestyle therapy for the control of excess weight.

Mazzoni et al., (2018) showed that both nutritional therapy and physical exercise had beneficial effects like those of cognitive-behavioral therapy in reducing bulimic symptoms.

Although the literature suggests a positive association between healthy weight control practices, such as physical activity and eating behaviors, few studies have explored physical activity or exercises to prevent, control or reduce symptoms of eating disorders (Holliday, 2017).

Activities that require prolonged activation of the aerobic mechanisms, that is, the ability of the cardiopulmonary system to supply oxygen to the muscles, especially those of high intensity ($\geq 60\%$ of the maximum volume of oxygen), commonly promote a transient suppression of appetite in eutrophic individuals, often associated with changes in appetite-regulating hormones (Mazzoni et al., 2018; Holliday, 2017).

Electrical brain stimulation or tDCS has been studied in recent years and has emerged as a promising neuromodulation technique in a

variety of clinical conditions (Fregni et al., 2018; Val-Laillet et al., 2015).

Neuroscience studies demonstrate that the modification in the activity of the dorsolateral prefrontal cortex (DLPFC) acts in a mechanism of general self-regulation of the domain and modulates affective and appetite self-regulation (Fregni et al., 2018; Val-Laillet et al., 2015).

In some studies, significant reductions in calorie intake were observed after active tDCS compared to its controls (Fregni et al., 2018; Val-Laillet et al., 2015).

Therefore, neuromodulation may be a possible approach to regulate food intake in patients with binge eating.

A systematic review that evaluated cognitive and neuromodulation strategies for unhealthy eating and obesity found that cognitive training and neuromodulation techniques affect neuroplasticity and combined interventions can generate a synergistic effect (Val-Laillet et al., 2015).

Therefore, non-pharmacological and non-invasive techniques such as aerobic exercise and tDCS can be used to control food intake as well as improving body composition and the combination of these techniques can allow the improvement of symptoms related to binge eating. In addition, some studies have shown that several stimulation sessions are necessary to achieve sustained changes in unhealthy eating (Howley et al., 1995; Ray et al., 2017).

However, considering the effect of tDCS on food desire and satiety and the effect of exercise on the same parameters (Ljubisavljevic et al., 2016; Burgess et al., 2016; Max et al., 2020), as far as we know, the combined techniques have not yet been investigated in a single session.

Thus, the aim of this study was to investigate whether a single session of tDCS alone or combined with aerobic exercise could reduce food consumption and the perception of hunger and satiety in patients with binge eating.

MATERIALS AND METHODS

Experimental draw

We conducted this randomized, double-blind, placebo-controlled study. All study procedures were approved by the Research Ethics Committee of our institution, and the study was registered with RebeC (RBR-

3d8fd2). A timeline with the experimental design of the study is shown in Figure 1.

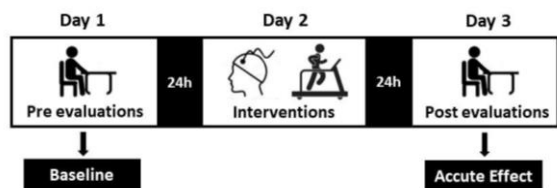


Figure 1 - Experimental design of the study.

Participants

Participants were recruited through public announcements and asked to complete an electronic questionnaire for initial screening according to the inclusion and exclusion criteria.

The inclusion criteria were being between 20 and 49 years, grade I overweight or obesity according to World Health Organization-WHO criteria (Holliday, 2017), binge eating diagnosis according to Diagnostic and Statistical Manual of Mental Disorders-DSM-5 criteria (Magno et al., 2014), and not having exercised regularly for 6 months.

The exclusion criteria adopted were to be nutritional monitoring or intervention, women intending to become pregnant, pregnant or breastfeeding women, history of severe depression or other serious psychiatric comorbidities, use of appetite-suppressing drugs, history of cardiovascular disease, renal failure, diabetes mellitus and inability to exercise.

Screening, randomization and general procedures

Participants who met the inclusion criteria in the screening were invited to perform the initial assessment, where they signed the informed consent form.

For the initial evaluation, they were instructed to perform an eight-hour fast and to prepare for the analysis of body composition, such as suspending calcium medications 24 hours before and not undergoing physical training on the day of the evaluation.

Initial assessments included: blood collection, body composition assessment (Dual-Energy X-ray Absorptiometry-DXA), maximum oxygen consumption test (VO_2 peak), food intake through the 24-hour food recall, visual analogue scales to assess hunger and satiety throughout the day, hunger at the time of testing

and uncontrollable desire to eat. An independent researcher randomly designated the treatment condition of each subject by drawing envelopes.

Thus, participants were randomized into three experimental groups: (1) active tDCS only - tDCS group, (2) active tDCS with AE-tDCS + AE group and (3) placebo tDCS with AE - tDCSpl + AE group. In the tDCS group, the subjects were submitted to 20-minute tDCS session. In the tDCS + AE group, the subjects were submitted to 20-minute tDCS session and then performed an aerobic exercise protocol for another 20 minutes. In the tDCSpl + AE group, the subjects were submitted to the same 20 minutes of tDCS, but it remained active for 30 seconds and afterwards the current was blocked and then the subjects performed the aerobic exercise protocol for another 20 minutes. The study was blinded to participants and evaluators.

Evaluation procedures

Biochemical markers

Venous blood samples were collected in anticoagulant tubes containing 4 mL EDTA after an overnight fast of at least eight hours. The tubes were centrifuged and plasma aliquots frozen at $-80\text{ }^{\circ}\text{C}$ for further analysis. Glucose levels (mg/dL), total cholesterol (mg/dL), high-density lipoprotein-HDL (mg/dL), triacylglycerol (mg/dL) and glycated hemoglobin (%) were measured using an automatic analyzer (Cobas C111, Roche Diagnostics, Basel, Switzerland), while low-density lipoprotein-LDL was calculated using the Friedewald equation. Plasma levels of insulin ($\mu\text{UI}/\text{mL}$) and leptin (ng/dL) were determined by ELISA, according to the manufacturer's instructions (BosterBio, Pleasanton, USA).

Assessment of food intake, hunger at the time of testing, hunger and satiety throughout the day and uncontrollable desire to eat

Food consumption was assessed by means of a 24-hour recall, with all food consumed in the 24 hours prior to the assessment being recorded, including the type of food and the amount consumed.

Food intake was assessed 24 hours before the start of the protocol and 24 hours after the session of the experimental protocol.

The total energy (Kcal) and the composition of macronutrients: carbohydrates, proteins and lipids (g) of the intake were calculated using the Dietbox® program. Hunger and satiety throughout the day and desire were measured twice (pre and post-interventions) with a subjective visual analog scale (VAS) that ranged from 0 to 10. Hunger at the time of the test was assessed in the same way, however, on a scale that ranged from 0 to 7.

Maximum oxygen consumption

The VO₂ peak and maximum heart rate (HRmax) of the participants were determined using an incremental exercise test on a treadmill (Inbramed, Porto Alegre / Brazil). The test started with a 5min warm-up (from 3 to 5 km / h, increasing 0.5 km / h each min, up to 5 min), followed by increases of 2% in the inclination every min, maintaining a constant speed of 5 km / h throughout the test.

To be considered a maximal stress test, participants should have met at least two of the following criteria: (1) HRmax predicted by age, (2) respiratory exchange ratio (RER) ≥ 1.1, (3) subjective perception of effort ≥ 17 (Borg scale 6-20), (4) signs of muscle fatigue, such as loss of motor coordination.

Ventilatory parameters were measured continuously, breath by breath, using an open circuit spirometry system (Quark CPET, Cosmed Italy) calibrated according to the manufacturer's instructions before each test day. HR was also measured continuously using chest strap telemetry (Polar Electro Oy, Kempele, Finland). VO₂ peak was identified as the highest VO₂ value in a trend line plotted against time. Participants were verbally encouraged to make the maximum effort during the test (Val-Laillet et al., 2015).

tDCS procedures

Participants were instructed not to eat at least two hours before the intervention, which they hoped to increase the degree of desire during the tDCS session. We used a stimulator model no. 1300A (Soterix Medical®).

The direction to the stimulation site (Dayan et al., 2013) was performed from the anode or cathode positioned in area F3 or F4, respectively, according to the international electroencephalogram (EEG) system 10-20. This method of locating the DLPFC was previously used in studies with tDCS for craving

(Fregni et al., 2018). The reference electrode was positioned in the contralateral supraorbital region.

Active tDCS group: tDCS was administered at 2mA for 20 minutes, configuring the treatment session.

Placebo tDCS group: the placebo system used in this study was that of the equipment itself, in which the sensation of active tDCS is imitated during the initial 30 seconds and subsequently stopped.

Virtual reality environment: using virtual reality glasses (Oculus®), structured exposure of images of foods that usually cause cravings (sweet, salty, fatty) was used simultaneously with the tDCS session.

Aerobic exercise protocol

The aerobic exercise was performed on a treadmill (BF 601-Oneal) immediately after each tDCS session for the tDCS + AE group. The training started with five minutes of warm-up at a comfortable speed on the treadmill. Subsequently, aerobic exercise was performed with intensity related to the percentage of VO₂ peak and monitored throughout the session by a frequency meter and subjective scale of perceived exertion (Borg Scale 6–20) (Howley et al., 1995).

The individuals performed 20 minutes with intensity of 60-65% of HRmax and subjective perception of effort from 12 to 14. At the end of each session, five minutes of stretching for the lower limbs were performed.

Sample calculation and Statistical analysis

The sample size calculation was based on the article by Lapenta et. al. (2014), which verified the effect of two sessions of tDCS (active or placebo) on calorie intake. The program used for the calculation was G * Power 3.1.9.2®, with $\alpha = 0.05$, $1-\beta = 0.8$ and effect size (f) = 1.0, totaling 30 participants, divided into three groups (10 per group). The statistical treatment took place according to the type of variable and distribution. Normality was analyzed using the Shapiro-Wilk test. The variables are described as mean ± standard deviation or median (first quartile - third quartile). Intergroup comparisons were performed by one-way ANOVA and Kruskal-Wallis test followed by Post hoc by Least Significance Difference (LSD). The intra-group comparisons were performed using the

dependent t test and the Wilcoxon signed rank test and Pearson's R. All analyzes were performed in SPSS v.21.0, except for the size of the R effect calculated in Microsoft Excel 2010. The level of significance was set at 0.05.

RESULTS

Characteristics of the participants

Characterization data for the participants are listed in Table 1. The sample consisted of eligible patients who underwent all protocols.

Table 1 - Characterization of the sample (baseline).

Variables	Active tDCS (n=11)	Placebo tDCS + AE (n=7)	Active tDCS + AE (n=11)	p value
Body composition				
Age (years)	35.5±9.2	38.0±5.9	34.7±8.1	0.70
Weight (Kg)	79.3 (72.7-83.2)	76.2 (68.6-95.9)	81.9 (76.4-97.5)	0.24
BMI (Kg/m ²)	29.9±2.5	29.4±3.5	30.9±2.0	0.49
Percentage of body fat (%)	43.8 (42.4-45.3)	43.6 (40.8-46.8)	43.6 (42.0-45.7)	0.85
Fat mass (Kg)	48.0±4.6	49.5±4.1	46.5±8.3	0.61
Lean mass (Kg)	49.8±3.3	46.1±3.9	43.2±6.3	0.01*
Total densitometry (BMD) (g/cm ²)	1.2±0.1	1.2±0.1	1.3±0.1	0.18
Maximum oxygen consumption test				
VO ₂ peak (mL/kg/min)	30.6±5.1	31.7±4.8	32.8±5.3	0.61
Maximum heart rate (bpm)	179.5±16.1	180.4±14.3	175.9±15.4	0.80
Biochemical analyze				
Glucose (mg/dL)	102.7 (94.0-118.2)	94.4 (92.1-104.8)	95.6 (88.3-100.0)	0.22
Insulin (μUI/mL)	20.4 (19.1-26.6)	17.7 (15.1-26.5)	23.7 (15.3-68.4)	0.63
Glycated hemoglobin (%)	5.8 (5.7-5.8)	5,6 (5.2-5.9)	5.8 (5.7-6.1)	0.34
Total cholesterol (mg/dL)	174.4 (130.1-183.4)	181.9 (170.9-190.8)	201.2 (160.6-217.6)	0.31
Triglycerides (mg/dL)	93.0 (55.0-120.1)	118.4 (89.7-145.8)	113.4 (89.5-120.7)	0.59
LDL-cholesterol (mg/dL)	77.2 (67.4-110.7)	105.8 (90.8-120.5)	104.4 (92.6-121.7)	0.22
HDL-cholesterol (mg/dL)	54.9±11.3	53.2±8.5	51.2±14.5	0.77

tDCS-Transcranial direct current stimulation; AE-Aerobic exercise; BMI-Body Mass Index; BMO-Bone mineral density; VO₂peak-Peak oxygen volume; LDL-cholesterol- Low density lipoproteins; HDL-cholesterol- High density lipoproteins. * p<0.05.

Food consumption

The treatment conditions did not significantly change the intake of energy or macronutrients in the intergroup and intragroup comparisons.

Assessment of hunger at the time of testing

Values were found to be very close to being detected with statistically significant differences. Large effect sizes can be observed and suggest that a larger sample would indicate a significant decrease in values especially for

individuals who are hungrier at the time of testing.

Assessment of uncontrollable desire to eat (desire for food)

No variable showed any difference between the groups at the baseline. Participants who received active tDCS had only less uncontrollable desire to eat tasty foods [8.0 (5.0-10.0) vs. 3.0 (2.0-8.0), p<0.05], however, with no differences in intergroup comparisons. The results of hunger at the time of the test and an uncontrollable desire to eat are described in Table 2.

Table 2 - Responses to visual analog scales (VAS) of hunger at the time of testing and uncontrollable desire to eat by adults with BED before and after a single session of tDCS and aerobic exercise. Analyzed by groups: active tDCS (n = 11), placebo tDCS + AE (n = 7) and active tDCS + AE (n = 11). Total (n = 29).

Variables	Group	Pre	Post	Intergroup comparisons P value	Intragroup comparisons P value	Effect size (R)
Hunger at the time of testing	Active tDCS	2.0 (1.0-3.0)	3.0 (2.0-5.0)		0.03*	
	Placebo tDCS + AE	3.0 (1.0-5.0)	2.0 (1.0-3.0)	0.08	0.07	0.91
	Active tDCS + AE	2.0 (1.0-4.0)	3.0 (3.0-5.0)		0.36	0.32
Candy Desire	Active tDCS	5.0 (0.0-9.0)	2.0 (0.0-7.0)		0.11	0.53
	Placebo tDCS + AE	3.0 (0.0-8.0)	3.0 (2.0-6.0)	0.93	0.71	0.18
	Active tDCS + AE	6.0 (0.0-8.0)	4.0 (2.0-5.0)		0.24	0.45
Salty Desire	Active tDCS	8.0 (5.0-10.0)	5.0 (2.0-8.0)		0.11	0.53
	Placebo tDCS + AE	7.0 (0.0-8.0)	7.0 (4.0-9.0)	0.40	0.59	0.24
	Active tDCS + AE	6.0 (5.0-8.0)	5.0 (2.0-6.0)		0.17	0.42
Tasty Desire	Active tDCS	8.0 (5.0-10.0)	3.0 (2.0-8.0)		0.04*	0.69
	Placebo tDCS + AE	8.0 (7.0-10.0)	7.0 (5.0-10.0)	0.36	0.19	0.64
	Active tDCS + AE	8.0 (5.0-9.0)	6.0 (3.0-9.0)		0.35	0.29
Fatty Desire	Active tDCS	4.0 (1.0-9.0)	2.0 (0.0-7.0)		0.11	0.57
	Placebo tDCS + AE	5.0 (4.0-8.0)	3.0 (2.0-6.0)	0.72	0.14	0.66
	Active tDCS + AE	3.0 (0.0-5.0)	2.0 (0.0-5.0)		0.73	0.13

tDCS-Transcranial direct current stimulation; AE-Aerobic exercise. * p<0.05.

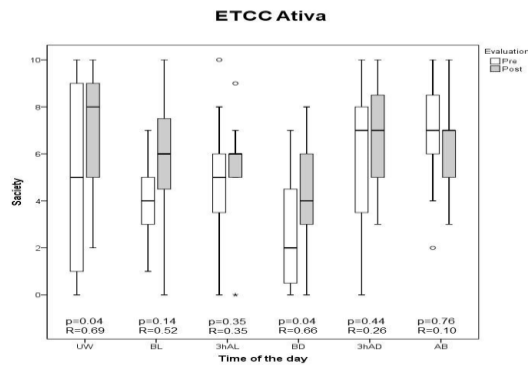
Assessment of hunger and satiety throughout the day

The analysis of the acute effect showed that the active tDCS group improved the assessments upon awakening [5.0 (1.0-9.0) vs. 8.0 (5.0-9.0), p<0.05].

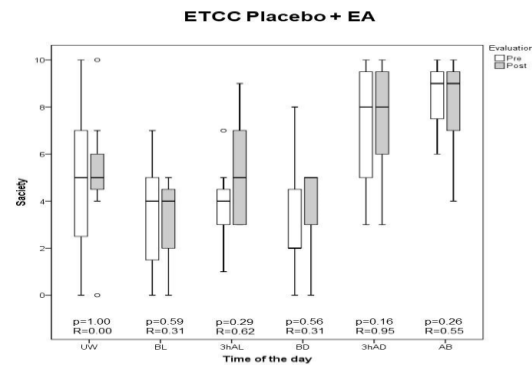
In addition, active tDCS with aerobic exercise significantly reduced hunger, that is, increased satiety, before dinner [1.0 (1.0-3.0) vs. 4.0 (4.0-7.0), p<0.01]. There were no

significant effects on comparisons between groups. Great effect magnitudes ($r > 0.80$) could be observed for hunger and satiety in the moments before dinner (active tDCS + AE), 3 hours after dinner (tDCS placebo + AE) and for hunger at the time of the test (placebo tDCS + AE). The results of hunger and satiety throughout the day can be seen in Figure 2.

Active tDCS



Placebo tDCS + AE



Active tDCS + AE

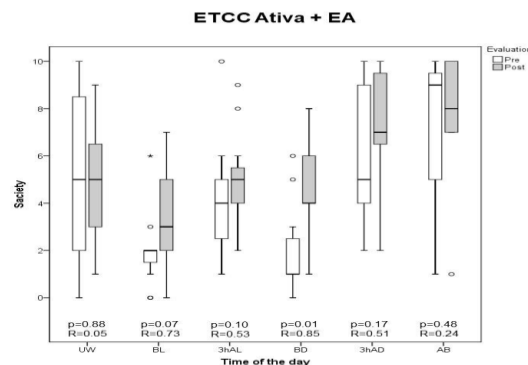


Figure 2 - Visual analog scale to assess satiety throughout the day. tDCS-Transcranial direct current stimulation; AE-Aerobic exercise; UW-Upon waking up; BL- Before lunch; 3hAL- 3h Before lunch; BD- Before dinner; 3hAD- 3 hours after dinner; AB- At bedtime. * $p < 0.05$.

DISCUSSION

Our study had two main findings: 1) the tDCS group had lower values of lean mass compared to the other groups; 2) in relation to food intake, hunger, satiety throughout the day, and uncontrollable desire to eat, tDCS alone or combined with exercise were equally effective.

The tDCS had no independent or synergistic effect on food intake, the same observed in a study with overweight individuals with binge eating (Burgess et al., 2016).

A recent study, using the same positioning of the electrodes as ours, showed that obese individuals who received anodic tDCS from the left DLPFC tended to have lower caloric intake and lose more weight than with

cathodic tDCS (Gluck et al., 2015; Heintz et al., 2017).

The isolated application of active tDCS generated the greatest number of changes in the investigated outcomes, increasing satiety at the time of the test, satiety on waking up and before dinner and decreasing the uncontrollable desire for tasty foods.

However, these changes were not sufficient to characterize a difference between groups, probably due to the sample size and data dispersion. A joint tDCS intervention with aerobic exercise increased satiety before dinner.

Although this difference was also detected in the active tDCS group, the effect size found is larger for the active tDCS + AE group, indicating a possible synergy for this

variable only. The tDCS placebo + AE group does not change in any outcome indicating that a single session of aerobic exercise is not able to cause changes and ruling out a placebo effect of tDCS.

Hunger measured at the time of the test showed a significant reduction in the tDCS group and approached a significant result in the tDCS placebo + AE group, with a large effect size.

Perhaps different results could be observed if the sample was larger. At the same time, in the uncontrollable desire to eat, a reduction was observed only in the active tDCS group for tasty foods. Interestingly, the other food groups did not have the same effect. This may be associated with being a food group of greater preference for individuals and, consequently, of greater consumption, but this factor was not controlled in our study.

Chen et al., (2019) conducted a study that explored the effects of a single anodic tDCS session on food cravings and found that individuals who received stimulation demonstrated higher levels of inhibition of the response to food after the intervention (Burgess et al., 2016).

In the analysis of hunger and satiety throughout the day, we observed a reduction in hunger when waking up in the group that received only tDCS, a result similar to that found by Fregni et al., (2018) who observed a reduction in the desire to eat right after a single session of tDCS. In our study, this group always performed the protocol early in the morning, which may have influenced satiety throughout the day. In our study, there was also a reduction in hunger before dinner for the tDCS + AE group, and this group always performed the protocol at the end of the day. Studies indicate that subjective feelings of appetite are temporarily suppressed during exercise performed at or above 60% of peak oxygen consumption (VO_2 peak) (King et al., 2010; Broom et al., 2007; Broom et al., 2009; Martins et al., 2007; Ueda et al., 2009; King et al., 2015) and increases in satiety hormone concentrations (PYY, GLP-1 and PP), were reported during aerobic exercise sessions with 65% maximum heart rate for ~ 60min (Broom et al., 2009).

However, perceptions of appetite as well as hormonal fluctuations related to satiety usually return to baseline values 30 to 60 minutes after stopping exercise, which can modify the perception of hunger (King et al.,

2010; Broom et al., 2007; Broom et al., 2009; Martins et al., 2007; Ueda et al., 2009; King et al., 2015).

Additionally, studies in overweight or obese individuals ($BMI \geq 25.0$ kg / m²) did not report any change in the perception of hunger during protocols of moderate and high intensity of acute aerobic exercise.

Martins et al., (2007); Larsen et al., (2007); Sim et al., (2014), as well as the concentrations of satiety hormones remained unchanged in the hours after exercise.

In addition, a study showed that in habitually low-active individuals, appetite and food intake were not affected by a single walking session (Unick et al., 2010).

Thus, we believe that the characteristics of our sample (that is, overweight and sedentary individuals) can explain the subtle results found with the exercise on the evaluated parameters.

We believe that, because acute exercise reduces neuronal responses in food reward (Hagobian and Evero, 2012) increases sensitivity to satiety-related neuropeptides (Ropelle et al., 2010) and suppresses energy intake (King et al., 2010) while DLPFC anodic tDCS can suppress the desire for food, the two techniques combined could in one session improve symptoms of binge eating.

As eating behavior is an important component that can increase adherence to prescribed diets, we believe that the potential of tDCS and aerobic exercise to modulate eating behavior can contribute to better adherence to dietary treatment and, therefore, to weight loss and better quality of life.

The limitations of the study were the small sample size and the lack of biochemical measures to verify hunger and satiety. Thus, longitudinal studies can better clarify the effectiveness of this combined treatment in binge eating.

CONCLUSION

In conclusion, our study showed that a single tDCS session on the left DLPFC with virtual reality associated or not with aerobic exercise increased satiety at the time of testing, satiety upon waking, satiety before dinner and decreased craving for tasty foods.

However, no effect was found on energy and macronutrient intake for any intervention. This might be clarified using a bigger sample in future studies.

ACKNOWLEDGMENT

Universidade Federal do Rio Grande do Sul - UFRGS, for the financial support for carrying out the research.

STATEMENTS DECLARATIONS

Funding: The authors declare that no funding, grants or other support was received during the preparation of this manuscript.

COMPETING INTERESTS:

The authors have no relevant financial or non-financial interests to disclose.

REFERENCES

- 1-Broom, D.R.; Batterham, R.L.; King, J.A.; Stensel, D.J. Influence of resistance and aerobic exercise on hunger, circulating levels of acylated ghrelin, and peptide YY in healthy males. *American journal of physiology Regulatory, integrative and comparative physiology*. Vol. 296. Num. 1. 2009. p. R29-35.
- 2-Broom, D.R.; Stensel, D.J.; Bishop, N.C.; Burns, S.F.; Miyashita, M. Exercise-induced suppression of acylated ghrelin in humans. *Journal of applied physiology*. Vol. 102. Num. 6. 2007. p. 2165-2171.
- 3-Brownley, K.A.; Berkman, N.D.; Peat, C.M.; Lohr, K.N.; Cullen, K.E.; Bann, C.M. Binge-eating disorder in Adults: A Systematic Review and Meta-analysis. *Annals of internal medicine*. Vol. 165. Num. 6. 2016. p. 409-20.
- 4-Burgess, E.E.; Sylvester, M.D.; Morse, K.E.; Amthor, F.R.; Mrug, S.; Lokken, K.L. Effects of transcranial direct current stimulation (tDCS) on binge eating disorder. *The International journal of eating disorders*. Vol. 49. Num. 10. 2016. p. 930-936.
- 5-Chen, S.; Jackson, T.; Dong, D.; Zhang, X.; Chen, H. Exploring effects of single-session anodal tDCS over the inferior frontal gyrus on responses to food cues and food cravings among highly disinhibited restrained eaters: A preliminary study. *Neuroscience letters*. Num. 706. 2019. p. 211-216.
- 6-Dayan, E.; Censor, N.; Buch, E.R.; Sandrini, M.; Cohen, L.G. Noninvasive brain stimulation: from physiology to network dynamics and back. *Nat Neurosci*. Vol. 16. Num. 7. 2013. p. 838-44.
- 7-Fregni, F.; Orsati, F.; Pedrosa, W.; Fecteau, S.; Tome, F.A.; Nitsche, M.A. Transcranial direct current stimulation of the prefrontal cortex modulates the desire for specific foods. *Appetite*. Vol. 51. Num. 1. 2008. p. 34-41.
- 8-Gluck, M.E.; Alonso-Alonso, M.; Piaggi, P.; Weise, C.M.; Jumpertz-von Schwartzberg, R.; Reinhardt, M. Neuromodulation targeted to the prefrontal cortex induces changes in energy intake and weight loss in obesity. *Obesity*. Vol. 23. Num. 11. 2015. p. 2149-2156.
- 9-Hagobian, T.; Evero, N. Exercise and Weight Loss: What Is the Evidence of Sex Differences? *Current obesity reports*. Num. 2. 2012.
- 10-Heinitz, S.; Reinhardt, M.; Piaggi, P.; Weise, C.M.; Diaz, E.; Stinson, E.J. Neuromodulation directed at the prefrontal cortex of subjects with obesity reduces snack food intake and hunger in a randomized trial. *The American journal of clinical nutrition*. Vol. 106. Num. 6. 2017. p. 1347-57.
- 11-Holliday, A.; Blannin, A. Appetite, food intake and gut hormone responses to intense aerobic exercise of different duration. *The Journal of endocrinology*. Vol. 235. Num. 3. 2017. p. 193-205.
- 12-Howley, E.T.; Bassett, D.R.; Welch, H.G. Criteria for maximal oxygen uptake: Review and commentary. *Medicine and Science in Sports and Exercise*. Vol. 27. Num. 9. 1995. p. 1292-301.
- 13-King, J.A.; Garnham, J.O.; Jackson, A.P.; Kelly, B.M.; Xenophontos, S.; Nimmo, M.A. Appetite-regulatory hormone responses on the day following a prolonged bout of moderate-intensity exercise. *Physiology & behavior*. Num. 141. 2015. p. 23-31.
- 14-King, J.A.; Wasse, L.K.; Broom, D.R.; Stensel, D.J. Influence of brisk walking on appetite, energy intake, and plasma acylated ghrelin. *Med Sci Sports Exerc*. Vol. 42. Num. 3. 2010. p. 485-492.

15-Lapenta, O.M.; Sierve, K.D.; Macedo, E.C.; Fregni, F.; Boggio, P.S. Transcranial direct current stimulation modulates ERP-indexed inhibitory control and reduces food consumption. *Appetite*. Vol. 83. 2014. p. 42-48. doi: 10.1016/j.appet.2014.08.005.

16-Larsen, P.S.; Donges, C.E.; Guelfi, K.J.; Smith, G.C.; Adams, D.R.; Duffield, R. Effects of Aerobic, Strength or Combined Exercise on Perceived Appetite and Appetite-Related international journal of sport nutrition and exercise metabolism. Vol. 27. Num. 5. 2007. p. 389-398.

17-Ljubisavljevic, M.; Maxood, K.; Bjekic, J.; Oommen, J.; Nagelkerke, N. Long-Term Effects of Repeated Prefrontal Cortex Transcranial Direct Current Stimulation (tDCS) on Food Craving in Normal and Overweight Young Adults. *Brain stimulation*. Vol. 9. Num. 6. 2016. p. 826-833.

18-Magno, F.C.C.M.; Silva, M.Sd.; Cohen, L.; Sarmiento, L.dA.; Rosado, E.L.; Carneiro, J.R.I. Nutritional profile of patients in a multidisciplinary treatment program for severe obesity and preoperative bariatric surgery. *ABCD Arquivos Brasileiros de Cirurgia Digestiva*. Num. 27. 2014. p. 31-34.

19-Martins, C.; Morgan, L.M.; Bloom, S.R.; Robertson, M.D. Effects of exercise on gut peptides, energy intake and appetite. *The Journal of endocrinology*. Vol. 193. Num. 2. 2007. p. 251-258.

20-Max, S.M.; Plewnia, C.; Zipfel, S.; Giel, K.E.; Schag, K. Combined antisaccade task and transcranial direct current stimulation to increase response inhibition in binge eating disorder. *European archives of psychiatry and clinical neuroscience*. 2020.

21-Mazzoni, G.; Chiaranda, G.; Myers, J.; Sassone, B.; Pasanisi, G.; Mandini, S.; et al. 500-meter and 1000-meter moderate walks equally assess cardiorespiratory fitness in male outpatients with cardiovascular diseases. *J Sports Med Phys Fitness*. Vol. 58. Num. 9. 2018. p. 1312-1317.

22-Ray, M.K.; Sylvester, M.D.; Osborn, L.; Helms, J.; Turan, B.; Burgess, E.E. The critical role of cognitive-based trait differences in transcranial direct current stimulation (tDCS)

suppression of food craving and eating in frank obesity. *Appetite*. Num. 116. 2017. p. 568-574.

23-Relton, C.; Li, J.; Strong, M.; Holdsworth, M.; Cooper, R.; Green, M.; et al. Deprivation, clubs and drugs: results of a UK regional population-based cross-sectional study of weight management strategies. *BMC Public Health*. Vol. 14. Num. 1. 2014. p. 444.

24-Ropelle, E.R.; Flores, M.B.; Cintra, D.E.; Rocha, G.Z.; Pauli, J.R.; Morari, J.; et al. IL-6 and IL-10 anti-inflammatory activity links exercise to hypothalamic insulin and leptin sensitivity through IKKbeta and ER stress inhibition. *PLoS biology*. Vol. 8. Num. 8. 2010. p. e1000465.

25-Sim, A.Y.; Wallman, K.E.; Fairchild, T.J.; Guelfi, K.J. High-intensity intermittent exercise attenuates ad-libitum energy intake. *International journal of obesity*. Vol. 38. Num. 3. 2014. p. 417-422.

26-Ueda, S.Y.; Yoshikawa, T.; Katsura, Y.; Usui, T.; Nakao, H.; Fujimoto, S. Changes in gut hormone levels and negative energy balance during aerobic exercise in obese young males. *The Journal of endocrinology*. Vol. 201. Num. 1. 2009. p. 151-159.

27-Unick, J.L.; Otto, A.D.; Goodpaster, B.H.; Helsel, D.L.; Pellegrini, C.A.; Jakicic, J.M. Acute effect of walking on energy intake in overweight/obese women. *Appetite*. Vol. 55. Num. 3. 2010. p. 413-419.

28-Val-Laillet, D.; Aarts, E.; Weber, B.; Ferrari, M.; Quaresima, V.; Stoeckel, L.E.; et al. Neuroimaging and neuromodulation approaches to study eating behavior and prevent and treat eating disorders and obesity. *NeuroImage Clinical*. Num. 8. 2015. p. 1-31.

Corresponding author:

Milena Artifon.

milena.artifon@gmail.com

Travessa José Rampanelli, 115 - Apartamento 402.

Bairro São Roque, Bento Gonçalves, Rio Grande do Sul, Brasil.

CEP: 95705-278.

Recebido para publicação em 12/07/2023

Aceito em 14/10/2023