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APPLICATION OF DIRECT TRANSCRANIAL CURRENT AS NON-INVASIVE THERAPY IN EATING DISORDERS: AN INTERVENTION PROPOSAL

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Abstract. Transcranial direct current stimulation constitutes a promising technique for the treatment of psychiatric disorders such as nervous anorexia. The way of acting is through the regulation of brain activity applied mainly in the area of the dorsolateral prefrontal cortex. This paper reviews the principles of transcranial direct current stimulation through the electrodes and how the intensity, duration and type of application procedures influence the results; the pathogenesis of anorexia nervosa, the different areas that are altered in terms of its operation, as well as the studies carried out in the dorsolateral prefrontal cortex and the different experimental studies of treatment in this typology of patients using this technique in recent years. years. A possible intervention proposal is also exposed based on the evidence found in the different works reviewed, introducing some improvements, with the aim of making the effectiveness of treatment with tDCS more widely known in future research.

Keywords: transcranial direct current stimulation (tDCS), nervous anorexia, dorsolateral prefrontal cortex, treatment, pathogenesis.

APLICACIÓN DE CORRIENTE TRANSCRANEAL DIRECTA COMO TERAPIA NO INVASIVA EN TRASTORNOS DE LA CONDUCTA ALIMENTARIA: UNA PROPUESTA DE INTERVENCIÓN

Resumen. La estimulación transcraneal de corriente directa constituye una técnica prometedora para el tratamiento de trastornos psiquiátricos como puede ser la anorexia nerviosa. La forma de actuación es a través de la regulación de la actividad cerebral aplicada principalmente en la zona de la corteza prefrontal dorsolateral. En el presente trabajo se revisan los principios de la estimulación transcraneal de corriente directa a través de los electrodos y cómo influye la intensidad, la duración y el tipo de procedimientos de aplicación en los resultados; la patogenia de la anorexia nerviosa, las diferentes áreas que se encuentran alteradas en cuanto a su funcionamiento, asi como lo estudios llevados a cabo en la corteza prefrontal dorsolateral y los diferentes estudios experimentales de tratamiento en esta tipología de pacientes mediante esta técnica en los últimos años. Se expone también una posible propuesta de intervención basándonos en las evidencias encontradas en los diferentes trabajos revisados introduciendo algunas mejoras, con lo que se pretende dar a conocer con mayor profundidad la efectividad del tratamiento mediante tDCS en futuras investigaciones.

Introduction

Eating disorders are characterized by abnormal and harmful habits in the diet that often present comorbidity with important medical and psychiatric disorders, leading to a loss of quality of life and being able to reduce the duration of the same.

Within the category of eating disorders we can find different types of disorders related to eating habits, but with particular characteristics and specific in each of them, such as morbid obesity; diagnosed in people whose body mass index (BMI) is greater than 40 kg/m2 and anorexia nervosa (AN) which is defined by an extremely low BMI (<18.5 kg/m2) which presents morbid concerns related to weight and body image according to the DSM-IV (American Psychiatric Association, 1994). This latter eating behavior disorder is characterized by weight loss or failure in weight gain that leads to wasting. Both diseases have a significant impact on people's lives, albeit in different ways. Morbid obesity is a chronic and progressive disease with a prevalence of approximately 14%, which has comorbidity with cardiovascular disease, type 2 diabetes mellitus, osteoarthritis and various types of cancer. By contrast, 0.7–3% of the population (predominantly 10:1 in the female population) suffers from AN, this disorder is also associated with critical metabolism, endocrine and electrolyte imbalances, psychiatric comorbities and an even higher risk of mortality due to the high suicide rate in this type of disorder and the complexity of complications that may occur. In addition to these disorders is also Bulimia Nervosa (BN), characterized by recurrent episodes of binge eating and inappropriate compensatory behaviors. A binge consists of ingesting large amounts of food over a short period of time, experiencing a feeling of loss of control over your intake. Another feature of the BN refers to excessive concern for weight and figure; personal worth is judged almost exclusively on the basis of weight and figure (American Psychiatric Association, 1994). It is estimated to have an overall prevalence of 0.3% and can afflict up to 1% of women, presenting psychiatric comorbities such as anxiety and depression. Another of the eating behavior disorders with a high prevalence is binge eating disorder. (Lee, 2018). This disorder is defined as a lack of control over intake that manifests itself by eating large amounts of food over a discrete period of time. Bingeing causes great discomfort in the subject; these are not followed by compensatory behavior and must occur at least twice a week for at least 6 months. This disorder is more common among people with obesity than in people with normo weight, according to the DSM-IV (American Psychiatric Association, 1994).

A wide variety of treatments have been applied for eating disorders among the most used today; from conservative measures (diet, exercise, cognitive behavioral therapy) to medications (e.g. benzamphetamine, orlistat, rimonabant) and bariatric surgery (Roux-in-Y gastric bypass, adjustable gastric laparoscopic band, sleeve gastrotrectomy, vertical band gastroplasty) in the case of obesity. Of these options, bariatric surgery is the most effective treatment for rapid weight loss but it is still associated with approximately a 10–27% failure rate. Currently, for the treatment of AN the most commonly used are cognitive behavioral therapy (CBT), selective serotonin reuptake inhibitors (SSRIs) and neuroleptics. According to the data, the treatments available for AN are only likely to be effective. Pharmacological treatment plays a limited role as the primary treatment, but with rather poor efficacy, in addition 30% of patients with AN prove to be medically intractable. Psychological therapies, such as CBT and family psychotherapy, are widely considered the treatment of choice. However, no individual psychological intervention showed a clear superiority in the treatment of adults with AN, while in adolescents with AN, the evidence base is stronger for the use of family psychotherapy on the individual than individual psychotherapies (Constanzo et al., 2018). In particular, the application of an integrated multifocal treatment, based on family and individualized psychotherapy, nutritional and pharmacological interventions, showed improvement in bedtime behaviors and psychopathology in adolescents with AN (Laghi et al., 2017). However, there is a need to continue efforts to develop novel interventions (Bodell and Keel, 2010). The situation is similar for BN; patients are typically treated with CBT and/or antidepressants (SSRIs) as pharmacotherapy, but most patients say they remain symptomatic after treatment.(Lee, 2018). As for treatment for binge eating disorder, it doesn't differ much from those listed above.

As we have mentioned, there are currently a wide variety of treatments for different disorders of eating behavior, but none of them have a high effectiveness, due to the high incidence of this type of disorder and the low percentage of recovery, different complementary treatments to those already existing are currently being studied. It is worth noting the low percentage of recovery and the high level of relapse that occurs in patients with ER, this accompanied by the large number of complications that come with an ER. In recent times are studying a variety of treatments that can help in the aspects discussed, among the procedures being investigated are techniques that can be used to stimulate or inhibit neuronal activity, this type of technique has been postulated as a potential treatment (McClelland et al., 2013; Lee et al., 2018).

The objective of this study is to analyze the different applications that have been carried out to date of neuromodulation techniques, in particular transcranial stimulation with direct current (tDCS), in patients with anorexia nervosa and to make a proposal for intervention.

Neuromodulation and pathogeny of eating disorders

Neuromodulation, is one of these potentially beneficial techniques, involves modifying the specific activity of the neural circuit without causing damage to nerve tissue, which involves the recovery of the previous functional state after discontinuation of the stimulus. This technique aims to activate or deactivate neural networks by applying a controllable electrical current with respect to frequency, amplitude and pulse width. It has been proposed as an alternative to the surgical procedures that were being applied in different pathologies. Experimental models have shown that high-frequency electrical stimulation affects the entire neural system, altering its metabolism and modifying neurotransmitter production and even protein synthesis. (Jáuregui-Lobera, 2018).

Among the different types of neuromodulation is noninvasive brain stimulation (NIBS) that involves transcranial cortical stimulation of neural targets in a non-surgical way. There are different types of stimulation; repetitive transcranial magnetic (rTMS) and transcranial direct current stimulation (tDCS) that are the most popular and frequently studied. These are non-invasive, focal, painless and safe brain stimulation techniques, the therapeutic potential of which underlies the ability to induce transient changes in cortical excitability status, in the case of rTMS; neuromodulation and brain plasticity, in the case of tDCS.

Each differs in terms of its stimulation mechanism; RTMS passes brief pulses of current through a coil over the scalp generating an electromagnetic field that inhibits (low frequency, <5 Hz rTMS) or active (high frequency,> 5 Hz rTMS) target neurons, while tDCS consists of stimulating with weak current electricity certain regions of the brain through electrodes placed on the scalp to depolarize (anodic tDCS) or hyperpolarize (cathode tDCS) resident neurons.

Both rTMS and tDCS have been explored with different successes for a multitude of disorders, including OCD, depression, anxiety, chronic pain, stroke rehabilitation, addictions and have also been applied to eating disorders (Jáuregui-Lobera, 2018).

The appeal of tDCS as a therapeutic intervention is multifactorial: it is safe and tolerable, non-invasive, producing mild side effects, such as paresthesia and erythema located at the stimulation site. The application of tDCS involves the placement of two patch electrodes on the scalp soaked in saline to promote electrical conduction. Low-intensity dc current (between 1-2.5 mA) is administered for a variable period between 10 and 30 minutes. This electric current produces a stimulation that results in partial depolarization of neural cell membranes in regions close to the anode and hyperpolarization near the cathode, causing a change in the spontaneous rate of neural triggering, thus modulating cortical excitability.

Anodic stimulation reduces the trigger threshold for the spread of action potentials, facilitating activity, while cathodic stimulation inhibits activity. Interestingly, the effect of tDCS depends on the direction of the current flow (i.e. parallel or perpendicular to the orientation of the underlying pyramid neurons). Due to the folding of the neocortex, the dominant current flow is perpendicular to the neural columns, so the mechanism of action of tDCS is mainly due to the polarization of synaptic terminals. The influence of the current direction and the importance of the polarity of the electrode with respect to the facilitation or inhibition of cortical activity reflects the relevance of the placement of the same to achieve the desired results of tDCS. (Dalton, 2018; Moffa, 2018).

To know where this type of treatment may be most beneficial it is necessary to know the pathogeny of ER, it is known that there are a number of brain regions involved in the regulation of homeostatic and hedical aspects of food behavior. Hypothalamic nuclei are essential for maintaining energy homeostasis, while limbic and cortical structures are involved in the non-homeostatic search for food in areas of reward and pleasure (Michaud, 2017). Irregularities in neural activity within homeostatic circuits may play an important role in the food deregulation of the eating disorders discussed above. There is evidence that certain forms of addiction and food cravings that are present in obesity share similar underlying mechanisms, such as deregulation of dopaminergic activity in the Mesolimbic pathways (Michaud, 2017; Monteleone, 2018). Research on the pathogenesis of AN and BN has also pointed to the deregulation of non-homeostatic reward pathways as a causal factor in the mechanism of development of ACT (Dalton, 2018; Jáuregui-Lobera, 2018; Surowka, 2018). The dorsolateral prefrontal cortex (dlPFC) has been identified as a key brain region involved in the regulation of food and behaviors in all eating behavior disorders, playing a critical role in both executive function, inhibitory control, integration of reward signals, and planning and execution of targeted behaviors (Costanzo , 2018; Ehrlich et al., 2015; Gordon, 2019; Hestad et al., 2016; Kekic, 2017; Lowe, 2017; Macedo, 2016; Ray, 2019). Associations between obesity and decreased functional activity in the lateral regions of the prefrontal cortex have also been observed after a meal by elucidating a potential mechanism that contributes to the development of obesity. This executive dysfunction can also worsen as a result of obesity, creating a negative feedback cycle that can make it difficult for obese people to change their eating behaviors. (Volkow ND, 2013).

One of the annotated characteristics of AN is comorbidity with affective disorders such as depression or bipolar disorder. Previous imaging studies suggest that AN involves dysfunction within several neural pathways, including circuits related to self-awareness (parietal cortex, insula), visual and taste sensation (occipital cortex and insula) and reward (ventral striated body, anterior and subcallosal cingulated body), dorsolateral PFC and ventromedial PFC. (Ellison et al., 1998; Val-Laillet et al., 2015; Zhang et al., 2013). Insula, which preserves interoception (an individual's self-observation of the body's internal homeostasis), is involved in many of these circuits and can be particularly related to distorted perceptions in AN.

A theory of the pathogenesis of AN suggests that there is an imbalance in the serotonergic signaling within the ventral striatum, perhaps related to the aversion aspect of the disorder (Taghva, Corrigan and Rezai, 2012). Another theory is the existence of disturbances in the reward pathways (Kaye and Bailer, 2011; Kaye, Fudge and Paulus, 2009; Kaye et al., 2013). Disruption of the dopamine system is known to affect reward circuits, leading to a dysphoric mood and anxiety (Kaye et al.,2013). There is evidence of a dopamine imbalance in the ventral striatum in patients with AN showing a decrease in activity as well as hyperactivity in the caudate (Wagner et al., 2007). In addition, the reward pathways of ED patients are triggered by disease-related stimuli, but are not necessarily activated with typical rewarding stimuli. For example, there is an overactivation of the ventral striatum in response to low weight stimuli (Fladung, Grang and Grammer, 2010).

Anorexia is associated with fronto-temporal hyperactivity of the right hemisphere (RH). Electroencephalography (EEG) measurements of people with anorexia showed an RH overactivation (Grunwald et al., 2004). Similarly, when performing a positron emission tomography (PET) scan to people with this eating behavior disorder, aimed at mapping serotonin activity around 5-HT1A receptors, larger groups of serotonergic junctions were found, predominantly in fronto-temporal regions of HR (Galusca et al., 2008). A review of anatomical and metabolic alterations of anorexia described the pathological profile as most often a posterior right hypometabolism, followed by a right anterior hypermetabolism, both associated with an abnormal electroencephalogram (EEG) peak of (RH Braun et al., 1992). In the same vein, patients with anorexia described drawings of healthy female body shapes, in different weight categories, as more aversive than the subject control group, and anorexic aversion ratings correlated positively with the activity of the right prefrontal cortex (Uher et al., 2004). In another study, they saw their own distorted images of the body and activated the right amygdala, the right fusiform turn, and the brainstem region, as if a "scarf" had been activated (Seeger et al., 2002).

Interest in the development of treatments targeting brain regions associated with appetite behaviors such as lateral prefrontal and subcortical regions, such as tDCS treatment, has increased in recent years. In general, the results support this treatment as a useful tool to potentially modify prefrontal cortex activity, food intake and weight intake and decreased anxiety. Brain stimulation techniques offer promising results in modulating food intake and eating behaviors. It has also been instrumental in helping to elucidate the underlying neuropathology and cognitive mechanisms that regulate appetitive behaviors.

Safety and efficacy of tDCS in anorexia treatments

Treatment with tDCS does not evoke action potentials, but induces a change in membrane potential, i.e. anodic stimulation causes depolarization of the membrane and increases the propensity for neuronal firing, while cathodic stimulation affects the probability of neuronal activity. (Phillipou et al., 2019). Consider a flexible treatment in terms of protocols and electrical dose, it is not easy to decide the most effective design for a given experiment. This is due in part to the current lack of comparable research available: there is great variability in protocol and configuration between published studies, and many of them are often underpowered due to small sample sizes (Berryhill et al. , 2014; Li et al., 2015).

The experiments carried out so far with tDCS in AN patients leave us with a variety of results.

In the first published study using this neuromodulation technique in patients with AN carried out by, Khedr, Elfetoh, Ali and Noamany (2014) stimulated the dorsolateral prefrontal cortex (DLPFC) with anodic tDCS in seven patients resistant to treatment with AN. Five patients showed improvement in eating disorder and depressive symptoms immediately after application for 10 days of tDCS, two of these patients maintained improvement at 1 month follow-up. Costanzo et al., (2018) also stimulated the left DLPFC with tDCS in a group of 11 participants (three sessions a week, for 6 weeks), also included a comparison group of 12 AN patients who received family therapy (FBT) in an open study. Although no group differences in eating disorder symptoms were reported, BMI was reported to increase significantly in the tDCS group, but not in the FBT group.

Results were obtained that were interpreted as a possible direct / indirect effect of tDCS in some pathophysiological mechanisms of AN, involving mesocortical dopaminergic pathways and increased food intake. This study first demonstrated a specific effect of a tDCS treatment on stable weight gain and superiority compared to an active control treatment for adolescents with AN. In the experimental group, tDCS was applied to the dlPFC and, more specifically, the anode electrode was placed on the left and the cathode electrode on the right area. According to the literature, this configuration, with concurrent left and right excitatory inhibitory stimulation, was applied to rebalance the right frontal hyperactivity reported in the AN (Bär et al., 2013; Brooks et al., 2011; Grunwald et al., 2004; Phillipou et al., 2015). Furthermore, all participants received nutritional and psychiatric follow-up, as well as psychological support. It is important to note that the two groups received a similar concurrent nutritional, psychoeducational and pharmacological treatment (the usual “as usual” AU treatment), which could have a major role in eating behavior and weight gain, while they differed for the specific complementary treatment (that is, the experimental tDCS or the treatment of choice FBT). This means that the results obtained can be explained by the complementary treatment or by the interaction between each complementary treatment and the AU treatment.

It is possible to speculate that treatment with tDCS may have a direct/indirect action on one of the aetiopathogenic mechanisms of AN and may represent a more specific treatment in perspective for AN, especially in adolescence. In fact, tDCS has the potential to timely detect brain abnormalities through brain plasticity mechanisms, essential in development. In reality, although "malleable" during the early stages, once established, AN patients are remarkably persistent (Constanzo, 2018; Walsh, 2013), therefore it is essential to treat the disorder early.

Very recently, the first human evidence has been published (Fonteneau et al., 2018) in which bifrontal tDCS induces the release of neurotransmitters in subcortical areas. Specifically, left/right cathodic-anodic tDCS, which induced a significant increase in extracellular dopamine in a part of the striatum involved in the reward-motivation network. Mesolimbic dopaminergic projections on the striatum are supposed to play a key role in governing eating behavior by modulating appetitive motivational processes. It has been hypothesized that disturbances in the dopaminergic reward (DA) pathways play a role in the pathogenesis of AN (Alcaro et al., 2007; Casper, 2006).

Therefore, one of the hypotheses is, although only speculatively, that the treatment used with left/right cathodic-anodic tDCS, aimed at rebalancing the hyperactivity of the right DLPC, can help to restore the cortical glutamatergic system that regulates the tonic DA in the striatum, acting in turn in the rebalancing of the dopaminergic alterations observed in the reward brain network in AN, crucial to regulate the behavior of food intake. (Constanza et al., 2018).

It is plausible that the positive effects found both in BMI and in psychopathological symptoms may arise from a synergistic action between cortical stimulation and medical stimulation in regulating the imbalance between the tonic and phasic component of DA in AN.

The application of tDCS in the right hemisphere is justified in the different studies based on the hyperactivation of said hemisphere. However, in the left hemisphere, DLPFC stimulation is largely justified based on studies in patients with major depression disorder, which generally stimulates this area, showing improvements, due to the great comorbidity that exists between this disorder of the mood and eating disorder. However, in healthy individuals, Vierheilig et al. (2016) with the aim of investigating the effects of bilateral tDCS with different electrode assemblies on the interaction of attention and emotion processes, they found that only left cathodic/right anode tDCS leads to increased visual attention, but neither left cathodic/right anode nor left anode/right cathode influenced emotional processing.

One of the latest studies by the Phillipou et al., (2019), concludes that anorexia is associated with abnormal HR. An adjunctive tDCS has good potential to facilitate recovery of patients with this condition, balancing the interhemispheric activity. As for the arrangement of the electrodes, an anode left and a cathode right onto the prefrontal is recommended for patients medicated with SSRIs, and DLPFC anode and a shoulder cathode contralateral (or other location noncephalic) it would be more appropriate for medicated patients with SSRIs. Along with nutritional supplements, psychotherapy and other treatments available.

In the different studies carried out, none of the subjects experienced significant side effects neither during the application nor afterwards. In one of the studies where tDCS side effects were most evaluated was in the study by Constanza et al., 2018, they were evaluated using a standard questionnaire (Brunoni et al., 2011) that participants completed after each stimulation session. The questionnaire lists adverse effects such as headache, neck pain, scalp pain, tingling, itching, burning sensation, skin redness, drowsiness, difficulty concentrating, and acute mood swings. Participants quantify the intensity of tDCS-related symptoms or side effects (1, absent; 2, mild; 3, moderate; 4, severe)

Regarding safety and tolerability, no participant requested to stop the study or reported significant discomfort at the electrode sites. The participants tolerated the application of tDCS well. The most frequent adverse effects were itching sensation, burning sensation (reported by 9 participants), especially in the first seconds of stimulation, which decreased rapidly with the addition of water under the sponge and local redness (report of 8 participants). Other effects were mild headache (reported by 5 participants), tingling (reported by 5 participants). This confirms a high tolerability and viability of a treatment with tDCS.

Current pilot studies

Currently, in the different databases consulted, two pilot studies carried out in the past year have been found, in which tDCS is used as a technique for the treatment of patients with AN.

One of the pilot studies is the one carried out by Phillipou et al., 2019 in Australia. Aiming to non-invasively stimulate the left lower parietal lobe (IPL) with HD-tDCS in individuals with AN, this pilot research provides preliminary evidence to determine the feasibility and acceptability of this type of treatment. One of the main differences with conventional tDCS is the application by means of high definition gel electrodes with large sponges.

In addition to presenting minimal physical risks, the duration of treatment with HD-tDCS has the potential to be significantly shorter than that required for psychological therapies in AN, such as CBT (i.e. 20 sessions for an estimated 20 weeks) (Phillipou et al. 2019).

For this study, 20 participants, women, diagnosed with AN, over 18 years of age and with a BMI (<18 km / m2), are selected, they must have been on stable pharmacological treatment for more than 1 month and the clinical situation at the moment it must be stable. Continuous medical assistance is required during the course of the intervention. Daily HD-tDCS (or simulated HD-tDCS) sessions were administered over 10 days (weekdays only) consisting of anodic HD-tDCS applied to the left IPL for 20 minutes at 2 mA (plus 30-second increase and 30-minute ramp down). seconds). The other mock HD-tDCS group was administered in the same manner, but the voltage decreased after the initial ramp from 30 seconds to 0. Similarly, it will rise and fall at the end of the 20 minute mock stimulation to replicate. ramp periods. While students are receiving HD-tDCS or HD-tDCS simulation, they will see visual distractors on a computer monitor.

The venue was the Melbourne Clinic (TMC) within the intensive day-to-day patient program for Body Image and Eating Disorders and Recovery Service (BETRS) at St. Vincent Hospital , Melbourne.

Efficacy assessment was performed using various assessment instruments, the eating disorder questionnaire (EDE-Q; short form), total scores, AN symptom scale scores (adapted from McClelland et al., 2016; Likert scale classifications that include impulse to eat, impulse to exercise, urge to restrict, feeling of fatness, feeling of fullness, mood and anxiety), and the rate of SWJ during a fixation task . Additionally, physical measurements (including BMI) and functional connectivity in the resting state of the left IPL were evaluated from the start to the end point of the treatment, as well as evaluations that have been previously reported in the literature as characteristics of AN that includes a battery of eye movement tasks (Phillipou et al., 2015; Phillipou, Rossell, Gurvich, Castle and Abel, 2016; Phillipou et al 2016; Phillipou, Rossell, Gurvich, Hughes, et al., 2016) Overall (ie, the Wisconsin Card Sorting Test). (Steinglass, Walsh and Stern, 2006). The evaluations were carried out both pretreatment with HD-tCDS and posttreatment, as well as a follow-up of 4 and 12 weeks.

The other pilot study is the one carried out by Strumila et al., 2019 in France, in which it was decided to carry out a pilot study using a method with a different design, varying the number of sessions. The primary objective of the study was safety and tolerability, and the secondary outcomes were efficacy and persistence.

The objective research subjects were ten female patients diagnosed with AN according to DSM-5, in serious condition, (that is, at least 3 years of progression with the failure of at least one of the outpatient treatments and a previous hospital treatment well performed by a specialized team) These patients were recruited at the eating disorders center of CHU Montpellier, France, being treated in a hospital setting, receiving the usual care, with pharmacological treatment of various kinds to manage the symptoms eaten. Subjects received 20 sessions of 2 mA andal stimulation for a period of two weeks (twice a day for 25 minutes, 10 days) in order to carry out a study differentiated from those that have been carried out until moment, incorporating an increase in the number of sessions that patients received (Strumila et al., 2019). The node was placed to the left of the DLPFC and the whole was placed to the right of the DLPFC in accordance with the international electrode placement system 10e20. The application of tDCS was combined with the usual multidisciplinary treatment of patients. During the two weeks of stimulation, none of the participants underwent a specific feedback protocol (i.e., nasogstric feedback), nutritional intervention, or assistance to a specialist psychological intervention group. In conclusion, nine out of ten patients with severe AN, completed the treatment protocol, without interruption in execution. The only patient who did not complete the protocol was for reasons other than stimulation.

There were no serious side effects, and some minor side effects in the andal stimulation zone disappeared quickly after the procedure. In terms of efficacy, significant improvements were observed in AN symptoms and improvements in compressed depression after the intervention and at one month of follow-up.

Propuesta de intervención

One of the essential conclusions of the studies is that given the lack of therapeutic options available in AN and the low cost of tDCS therapies, they could be performed safely in outpatient settings. Although it is true that these results require exhaustive research, they are necessary for the future and in a controlled and random way to confirm whether the application of tDCS could be a safe and effective complementary treatment option in patients suffering from AN.

Objective

Learning the effectiveness of the intervention with tDCS in patients with AN, diagnosed and with stable treatment. Subjects were divided into two groups: group 1 was given tDCS (treatment group) and group 2 was applied the electrodes and the same sessions as if they were receiving tDCS but without receiving it (sham or sham group). None of the subjects will be aware of whether they receive tDCS or simulated sessions previously. The evaluation of the results will be double-blind in such a way that the person in charge of analyzing the data will not previously know which subjects have received tDCS and which have not, since these are coded. The intervention with tDCS in group 1 patients will act as a complementary treatment to their usual treatment, both pharmacological and psychological.

HD-tDCS will be used for its greater precision and to facilitate the analysis of the data using fMRI (Esmaeilpour et al., 2019), placing the electrodes in the areas that have shown greater effectiveness; in the left dlPFC the node (excitatory) and in the right dlPFC the whole (inhibitory), the intensity will be 2mA, with a duration of 25 minutes, 15 sessions from Monday to Friday, alternate days, a total duration 5 weeks.

Evaluation

We propose to carry out this evaluation both in the pretreatment with tDCS and at the end of it in the following periods: one month, the third month, the sixth month and after one year. Various assessment instruments will be used, the eating disorder questionnaire (EDE-Q; short form), total scores, AN symptom scale scores (adapted from McClelland et al., 2016; Likert scale classifications that include the urge to eat, urge to exercise, urge to restrict, feeling of fatness, feeling of fullness, mood and anxiety). Additionally, physical measurements (including BMI) were evaluated.

In order to carry out a metabolic analysis of activity in the brain areas where tDCS is applied and to assess the changes and differences between the two groups and before and after the application of tDCS, an evaluation will be performed Randomized 6 of the participants in each group of brain activity using functional magnetic resonance imaging (fMRI). The fMRI data will be obtained before and after completing the stimulation session and always from the same subjects.

This evaluation will help us to correlate the effect of tDCS and the best of the subjects in the AN assessment tests, thus demonstrating that this improvement is an effect of tDCS in combination with classical treatment. The fMRI supports noninvasive images of brain function as the name implies, allowing the study of dynamic physiological changes (Symms, et al., 2006). Therefore, it allows us to study not only how stimulation modulates specific brain regions, but also how tDCS modulates activity throughout the brain in the context of anatomical and functional connectivity. In addition, this integration can also provide a critical insight into how, where and when stimulation is likely to be most effective, useful for optimization purposes.

In a methodological review carried out by Esmaeilpour et al, in 2019, 118 articles were analyzed where tDCS and fMRI were applied simultaneously in various cases, in order to explore the methodological parameters of integration n of tDCS with fMRI. The conclusion of this review about the use of the fMRI as a means of evaluation is positive, although it indicates that the way to do it must be very exhaustive and with a correct application to avoid the risk of induction of currents for sitas. These additional considerations will be taken into account for the correct evaluation of the data and as indicated to avoid risks.

Conclusions

Current AN treatments are expensive, many patients receive treatment for many years, and a large proportion do not achieve long-term recovery. Brain-stimulating techniques such as HD-tDCS, which are noninvasive and with negligible secondary risks, provide a promising potential therapeutic tool for the treatment of AN if they are effective as preliminary studies indicate.

The lack of exhaustive controlled and randomized research in addition to the reduced volume of these investigations means that this resource is not currently being used as part of the treatment in patients with AN (Berryhill et al., 2014; Li et al. , 2015). The easy accessibility and application of the intervention means that we must further study what is related to perfecting the application protocol in order to access this type of non-invasive neuromodulation treatment in an easier way in the future. It has been verified that the effects are always positive, and the secondary ones are hardly noticeable and of a very short duration.

It will only be through proposed interventions such as the one exposed in our article and future research after its application how we will be able to elucidate whether this type of treatment has real therapeutic value, as has been verified in other psychiatric disorders.

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