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## THE THERAPEUTIC PERSPECTIVE OF TRANSCRANIAL ELECTRICAL STIMULATION IN NEUROGENIC BLADDER IN CHILDREN WITH MYELOMENINGOCELE: A DESCRIPTIVE REVIEW

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**Introduction:** Myelomeningocele is a complex congenital malformation where the spinal cord, meninges and nerve roots are affected. Children with this malformation may present a bladder neuromuscular disorder called neurogenic bladder, the main symptom of which is urinary incontinence. Transcranial direct current stimulation (tDCS) has substantial scientific evidence in the treatment of various dysfunctions, by activating the regulation of the neural network, presenting a possible approach for the treatment of urinary incontinence in the pediatric population.

**Objectives:** Carry out a literature review on the effects of tDCS corresponding to the pelvic motor cortical area. Furthermore, describe the urinary neuromotor symptoms of myelomeningocele and their therapeutic possibilities within tDCS non-invasive neuromodulation.

**Methods:** A descriptive review of the literature was carried out using the academic databases Pubmed, Medline and Google Scholar, Lilacs, with descriptors in Portuguese and English, including material from November 2023 to April 2024, as well as neuromodulation and neurorehabilitation books.

**Results:** 14 articles and 8 books were initially found and, after screening, only 10 articles and 5 books had relevant potential to compose the descriptive literature review.

**Conclusion:** Data from the literature suggest that tDCS is a promising technique in childhood rehabilitation, with great therapeutic potential in the neurophysiological context. Considering the connection between the central nervous system axis and the peripheral innervations, the topic must be further studied in order to scientifically prove tDCS as an approach to rehabilitate pediatric urinary dysfunctions, as a safe and effective treatment option.

## THE SYNERGISTIC EFFECTS OF CYCLOSERINE AND ANODAL tDCS: A SYSTEMATIC REVIEW

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**Objectives:** This systematic review investigates whether Cycloserine (CYC), a partial N-Methyl-D-Aspartate (NMDA) receptor agonist, influences transcranial direct current stimulation (tDCS)-induced cortical excitability. We hypothesized that Cycloserine would augment the enhancement of cortical excitability elicited by anodal transcranial direct current stimulation due to their synergistic effects on NMDA receptors and improve clinical outcomes.

**Methods:** Evidence was gathered through an online search using Medical Subject Headings (MeSH) terms related to Cycloserine and transcranial direct current stimulation in PubMed, Embase, and Web of Science. The systematic review included studies examining the effects of Cycloserine combined with transcranial direct current stimulation, excluding animal studies.

**Results:** The review included one case report and five trials. One trial found that Cycloserine selectively prolonged the excitability increases induced by anodal transcranial direct current stimulation, with effects lasting up to 120 minutes post-stimulation. Another trial showed that motor-evoked potential amplitudes under Cycloserine were still enhanced the morning after stimulation compared to baseline values, suggesting a prolongation of excitability enhancement. However, another study demonstrated no significant change in cortical excitability after Cycloserine administration. Functionally, combining Cycloserine with anodal transcranial direct current stimulation reduced pain perception by 60% for up to 6 weeks, whereas the control saw only a 20-30% reduction, with effects fading after 2 weeks in a case report. The combination did not improve depression treatment efficacy in patients who had failed at least two adequate trials of antidepressants. Additionally, the combination did not improve motor learning, although transcranial direct current stimulation alone did not show improvement.

**Conclusion:** The findings are controversial but suggest that Cycloserine can prolong cortical excitability induced by anodal transcranial direct current stimulation. These mixed results underscore the necessity for further research into both the neurophysiological mechanisms and the clinical applications of Cycloserine and tDCS.

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## MINDFULNESS-BASED INTERVENTION IN MANAGING THE PAINFUL EXPERIENCE OF WOMEN WITH CHRONIC TMD

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**Objectives:** To analyze the effectiveness of an 8-week mindfulness-based intervention for managing the painful experience related to chronic temporomandibular disorder (TMD) in women.

**Methods:** Fifty-three women aged 18 to 65 with a TMD diagnosis according to the Diagnostic Criteria for Temporomandibular Disorder (DC/TMD) were randomized into either the mindfulness intervention group (IG) or the waitlist control group (CG). All participants underwent clinical evaluations and completed self-administered questionnaires regarding sociodemographic data, pain experience (BPI-B), stress, anxiety, and depression (DASS-21), pain catastrophizing (PCS), central sensitization (CSI-A), and mindfulness level (FFMQ) before and after the intervention period.

**Results:** Women in the IG showed a reduction in the number of familiar pain points at maximum mouth opening ( $\beta=-0.95$ , 95% CI: -1.75 to -0.16;  $p=0.02$ ), in the number of familiar ( $\beta=-4.10$ ; 95% CI: -6.53 to -1.67;  $p=0.001$ ) and referred pain points ( $\beta=-4.43$ ; 95% CI: -6.98 to -1.89;  $p=0.001$ ) during palpation; a significant increase in the pressure pain threshold at the average of body points ( $\beta=0.41$ ; 95% CI: 0.05 to 0.76;  $p=0.03$ ) and facial points ( $\beta=0.32$ ; 95% CI: 0.12 to 0.51;  $p=0.002$ ); a reduction in catastrophic thoughts ( $\beta=-7.56$ ; 95% CI: -12.83 to -2.28;  $p=0.006$ ) and stress levels ( $\beta=-2.61$ ; 95% CI: -4.96 to -0.27;  $p=0.03$ ); and an increase in dispositional mindfulness levels ( $\beta=15.81$ ; 95% CI: 4.79 to 26.82;  $p=0.006$ ).

**Conclusion:** Mindfulness-based intervention can contribute to the sensory, cognitive-behavioral, and emotional management of painful TMD.

## EXPLORATORY STUDY OF THE COGNITIVE ASSESSMENT OF WORKING MEMORY IN DEPRESSION IN THE ELDERLY AFTER THE USE OF REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION BY THE THETA-BURST METHOD: A RANDOMIZED DOUBLE-BLIND CLINICAL TRIAL

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**Introduction:** Repetitive transcranial magnetic stimulation (rTMS) is a non-pharmacological intervention used to treat major depressive disorder (MDD) (Blumberger et al., 2018). Theta burst stimulation (TBS), a modified rTMS protocol, provides cortical excitation with magnetic stimuli above 5 Hz, and has shown satisfactory results (Blumberger et al., 2018). With rising life expectancy, the growing elderly population's morbidities will become more significant public health concerns. Recent studies suggest that TBS does not impair the cognitive functions of patients and may even enhance cognitive performance (Moreno et al., 2015; Veiel, 1997). This can be evaluated using neuropsychological tests, such as the n-back test for working memory (WM).

**Objectives:** Investigate working memory in elderly individuals after TBS in an exploratory study.

**Methods:** This exploratory study investigated working memory in patients over the age of 60 treating for moderate depression. Twenty-three sessions of bilateral TBS were performed in the prefrontal region, continuous on the right and intermittent on the left. The 2-back test was used to assess WM before the TBS session and at the end of the 20 sessions, and repeated after 6, 8 and 12 weeks. Clinical variables were assessed using the Hamilton Depression Rating Scale, Montgomery-Asberg Depression Rating Scale and Geriatric Depression Scale. Cognitive variables were assessed using 2-back accuracy and reaction time (RT).

**Results:** The final sample consisted of 105 participants, 53 patients in the active and 52 in the sham protocol. Prior to the treatment, there were no significant differences ( $p > 0.05$ ) in age, education, gender, scales, accuracy and RT between groups. At the end of treatment, significant intra-group improvement in depressed symptoms were observed ( $p < 0.05$ ), but no changes were noted in 2-back test performance, including accuracy and RT ( $p > 0.05$ ). Comparisons between groups after treatment showed no significant differences in changes for depressive symptoms ( $p > 0.05$ ) or 2-back test performance ( $p > 0.05$ ).

**Conclusion:** After TBS intervention, both groups showed significant improvement in depressive symptoms, but no significant change in WM. To better understand the results, outcomes at follow-up will be evaluated.

## EFFECTS OF ROBOTIC THERAPY ON LOWER LIMBS MOBILITY IN POST-STROKE INDIVIDUALS

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**Objectives:** This study aimed to investigate the therapeutic effects of robotic therapy for lower limbs (LL) in stroke patients. Specifically, it sought to analyze how this intervention influenced knee and ankle movement, as well as to evaluate improvements in gait, balance, and motor coordination.

**Methods:** Participants underwent intervention of 45 minutes twice a week throughout nine weeks, totaling 18 sessions. The Vivax robot, developed for neurological and orthopedic rehabilitation, was used integrating virtual reality games to engage patients. In each session, the patient was seated in an adjustable chair and interacted with computer games while their foot was attached to the robot, which provided the necessary assistance, ensuring safe interaction.

**Results:** Five stroke survivors were evaluated, three of which (60%) completed the treatment. Two withdrew as they did not meet the inclusion criteria. The group had a male predominance (66.6%) and an average age of 67 years. Ischemic stroke (66.6%) and left-side involvement (66.6%) were most common. Reevaluation showed improvements on the Dynamic Gait Index (DGI), especially for patients 2 and 3, who increased by five and four

points, respectively. The Fugl-Meyer scale indicated improvements in lower extremity and coordination/velocity, except for participant 2, who showed no change. All participants maintained performance in passive joint movement and pain domains. The motivation questionnaire revealed that all participants (100%) enjoyed the therapy and would repeat it. Responses varied, with 33.3% reporting moderate or mild discomfort.

**Conclusion:** Robotic therapy for lower limbs was effective in improving mobility and motor coordination in post-stroke individuals, particularly in gait and motor control. Despite the small sample size, the results highlight its potential. Positive feedback suggests the therapy was well-received, though some discomfort was reported. Further research is needed to confirm its efficacy in larger samples and explore its impact on various recovery domains.

## EFFECTS OF HISTAMINERGIC COMPOUNDS ON NON-MOTOR FUNCTIONS IN AN ANIMAL MODEL OF PARKINSON'S DISEASE

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**Objectives:** This study aimed to investigate the participation of histamine H4 receptors in non-motor functions in an animal model that mimics PD (6-hydroxydopamine).

**Methods:** Forty mice (Swiss Albino) were divided into four groups (6-OHDA+VUF, 6-OHDA+saline, Sham+VUF, and Sham+saline) and submitted to neuronal injury induced by 6-hydroxydopamine (6-OHDA). The day after the injury, the animals received an acute dose of an H4 receptor agonist (VUF-8430) or vehicle and were followed for another thirteen days of recovery. The sucrose preference test, open field test, and tail suspension test were used for behavioral evaluation. Subsequently, the animals were euthanized by decapitation, and the brain and a blood sample were collected for molecular analysis (HPLC-EDC, ELISA, and Western Blot). For statistical analysis, the Shapiro-Wilk and Levene tests were performed for normality and homogeneity of variables, respectively, followed by the one-way ANOVA test. The significance level adopted was  $p < 0.05$ .

**Results:** Tukey's post hoc analysis identified a significant decrease in sucrose preference in the 6OHDA+VUF group compared to the Sham+VUF group ( $p=0.026$ ). In the open field test, there was a significant difference indicating a decrease in the number of total crossings and number of entries into the central zone in the 6-OHDA+VUF ( $p=0.000$ ) and 6-OHDA+saline ( $p=0.000$ ) groups compared to the Sham+VUF group. The time spent in the central zone did not show a significant difference. There was also no significant difference between the groups in the tail suspension test.

**Conclusion:** Our results indicated depression-like behavior in the lesion model associated with VUF-8430. In locomotor behavior, the results showed that both lesion groups had lower overall locomotor activity, while in the Sham group - that received VUF - this behavior was facilitated. Molecular analyses are necessary for further discussion and strengthening of the findings.

## ACUTE tDCS PROTOCOL REDUCES FOOD CRAVINGS IN WOMEN WITH OBESITY

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**Objectives:** Obesity is associated with a decreased brain activity in the dorsolateral prefrontal cortex, a relevant region for eating behavior. Increasing the activity of this area through transcranial direct current stimulation (tDCS) may help control food craving. The aim of this study was to test a new acute protocol to evaluate the effects of tDCS on food craving and anthropometric parameters in women with obesity.

**Methods:** This was a randomized, double-blind, sham-controlled clinical study, 22 women with obesity underwent a three-phase intervention: Phase 1 (target engagement), Phase 2 (acute tDCS protocol + nutritional intervention: five days with three daily sessions of 20 minutes, along with nutritional education during the intervals between the sessions), and Phase 3 (follow-up: monitoring of participants in the first, third, and sixth months after the intervention). Changes in food craving and anthropometric parameters were evaluated. Data were analyzed as linear mixed models with  $P < 0.05$ .

**Results:** Immediately after stimulation (Phase 2), a reduction in momentary food craving (FCQ-State) was observed in the active group ( $p 0.03$ ). Additionally, a reduction ( $p 0.003$ ) was also observed between the pre-stimulation (Phase 1) and the last phase of the study (Phase 3 at the sixth month) concerning more stable and enduring food craving (FCQ-Trait). There were no differences in anthropometric parameters.

**Conclusion:** Our results suggest that tDCS applied to the left dorsolateral prefrontal cortex seems to reduce food craving immediately after tDCS stimulation which remains after six months. However, tDCS did not facilitate weight loss or anthropometric changes.

## ACUTE EFFECT OF TRANSCUTANEOUS AURICULAR VAGUS NERVE STIMULATION AT TWO SITES ON CARDIAC AUTONOMIC MODULATION IN HYPERTENSIVE INDIVIDUALS: A PILOT STUDY OF A RANDOMIZED CROSSOVER CLINICAL TRIAL

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**Objectives:** This study aimed to compare the acute effects of transcutaneous auricular vagus nerve stimulation (tVNS) at two distinct sites on heart rate variability (HRV) in hypertensive individuals.

**Methods:** Fourteen adult hypertensive participants engaged in a 30-minute session of tVNS, administered over the tragus and the left cymba concha, with a one-week interval between sessions. The established parameters included a frequency of 30 Hz, a pulse width of 500  $\mu$ s, and an intensity ranging from 0.5 to 12 mA. HRV was assessed before, during, and after tVNS using the variables of low frequency (LF), high frequency (HF), and low frequency to high-frequency ratio (LF/HF).

**Results:** Cymba Concha Stimulation: A significant decrease in LF was observed (baseline:  $76.81 \pm 11.37$  vs. stimulation:  $70.38 \pm 11.87$ ,  $p=0.025$ ) and (baseline:  $76.81 \pm 11.37$  vs. post-stimulation:  $73.06 \pm 12.59$ ,  $p=0.060$ ). A significant increase in HF was noted (baseline:  $23.14 \pm 11.35$  vs. stimulation:  $29.58 \pm 11.85$ ,  $p=0.025$ ) and (baseline:  $23.14 \pm 11.35$  vs. post-stimulation:  $26.90 \pm 12.57$ ,

$p=0.058$ ). A decrease in the LF/HF ratio was found (baseline:  $4.552\pm 2.991$  vs. stimulation:  $2.867\pm 1.434$ ,  $p=0.042$ ) and (baseline:  $4.552\pm 2.991$  vs. post-stimulation:  $3.224\pm 1.278$ ,  $p=0.030$ ). However, no relevant changes were detected between stimulation and post-stimulation ( $2.867\pm 1.434$  vs. post:  $3.224\pm 1.279$ ,  $p=0.369$ ). Tragus Stimulation: No significant effects were observed for LF (baseline:  $72.47\pm 15.65$  vs. stimulation:  $74.84\pm 12.10$ ,  $p=0.559$ ) and (baseline:  $72.47\pm 15.65$  vs. post-stimulation:  $70.58\pm 13.62$ ,  $p=0.577$ ). No significant changes were found for HF (baseline:  $27.50\pm 15.64$  vs. stimulation:  $25.13\pm 12.10$ ,  $p=0.559$ ) and (baseline:  $27.50\pm 15.64$  vs. post-stimulation:  $29.38\pm 13.61$ ,  $p=0.578$ ). Additionally, there were no significant findings for the LF/HF ratio (baseline:  $3.567\pm 2.100$  vs. stimulation:  $3.886\pm 2.337$ ,  $p=0.640$ ) and (baseline:  $3.567\pm 2.100$  vs. post-stimulation:  $3.140\pm 2.019$ ,  $p=0.303$ ).

**Conclusion:** The results of this study suggest that transcutaneous auricular vagus nerve stimulation (tVNS) administered to the cymba concha produces a more pronounced modulation of heart rate variability (HRV) than tVNS applied to the tragus in individuals with hypertension.

## CORTICAL OXYHEMOGLOBIN DURING APNEA TASK IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS UNDERGOING HIGH-DEFINITION TRANSCRANIAL DIRECT CURRENT STIMULATION

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**Objectives:** To compare cortical oxyhemoglobin (OxyHb) concentrations during apnea task periods in the contralateral region to high-definition transcranial direct current stimulation (HD-tDCS).

**Methodology:** Twenty patients diagnosed with chronic obstructive pulmonary disease (COPD) were evaluated using functional near-infrared spectroscopy while receiving 3 mA HD-tDCS stimulation for 20 minutes on the left diaphragmatic motor cortex, with anodal, cathodal, and sham polarities. Patients were instructed to maintain a 10-second apnea period, alternating with 30 seconds of rest, for 10 cycles. A region of interest contralateral to the stimulation was defined and an average of the channels in this area was calculated.

**Results:** Repeated measures ANOVA revealed a significant difference in the effects of the three polarities on OxyHb concentration,  $F(2, 34) = 4.33$ ,  $p = 0.021$ . Post-hoc comparisons with the Bonferroni test showed that anodal current resulted in a significantly higher OxyHb concentration than sham ( $p = 0.046$ ). There were no significant differences in cathodal current.

**Conclusion:** Previous studies highlight cerebral hypoperfusion associated with hypoxia in COPD patients. Therapeutic alternatives such as HD-tDCS emerge as potential tools in treating this condition but need to be explored in neurophysiological terms. This study suggests increased oxygen metabolism during anodal current stimulation compared to sham during the hypercapnic task in a region outside the 4x1 spatial montage, highlighting the potential of anodal HD-tDCS in cerebral hemodynamics in this population.

## LACK OF COMPLEX MOTOR IMAGERY ABILITY AND PHANTOM LIMB PAIN: A SURROGATE FOR MOTOR CORTEX PLASTICITY RESERVE?

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**Background:** Individuals with amputation have a high prevalence of painful (PLP) and non-painful limb sensations (PLS) over a lifetime, and it has been suggested that phantom limb phenomena interfere with motor imagery ability due to loss of afferent information and brain reorganization.

**Objectives:** To investigate the relationship between motor imagery and phantom limb painful and non-painful sensations.

**Methods:** Detailed data from fifteen transradial amputees evaluated in the MeganePro project was acquired. The data collected were the motor imagery ability scores assessed using the Vividness of Movement Imagery Questionnaire-2 (VMIQ-2) as well as PLP and PLS measures.

**Results:** A significant positive correlation was found between total external visual imagery score and phantom pain magnitude ( $r=0.60$ ,  $P = 0.01$ ). In particular, a larger and stronger significant positive correlation was observed between the external visual imagery of the complex tasks, running ( $r=0.57$   $p=0.02$ ), jumping sideways ( $r=0.55$   $p=0.03$ ) and running downhill ( $r=0.65$   $p=0.001$ ). In addition, a significant positive correlation was found between external and internal visual imagery scores corresponding to the activity "swinging on a rope" and phantom limb sensation average.

**Conclusion:** Our findings suggest a potential protective effect against PLP in subjects with the ability for more complex types of motor imagery, thus suggesting this modality of imagery may be a surrogate for better motor engagement and plasticity.

## ACUTE EFFECT OF TRANSCUTANEOUS AURICULAR VAGUS NERVE STIMULATION AT TWO SITES ON CARDIAC AUTONOMIC MODULATION IN HEALTHY INDIVIDUALS: A PILOT STUDY OF A RANDOMIZED CROSSOVER CLINICAL TRIAL

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**Objective:** This study aimed to compare the acute effects of transcutaneous auricular vagus nerve stimulation (tVNS) at two distinct sites on heart rate variability (HRV) in healthy individuals.

**Methods:** Fourteen healthy adult participants underwent a 30-minute session of tVNS, applied over the tragus and the left cymba conchae, with a one-week interval between sessions. The stimulation settings were a frequency of 30 Hz, a pulse width of 500 $\mu$ s,

and an intensity range of 0.5 to 12 mA. HRV was evaluated before, during, and after the stimulation sessions, using the low-frequency (LF), high-frequency (HF), and LF/HF ratio as variables.

**Results:** Cymba conchae stimulation: LFnu increased from baseline ( $65.28 \pm 20.79$ ) to post-stimulation ( $71.44 \pm 19.43$ ),  $p=0.094$ , but decreased during stimulation ( $58.96 \pm 19.81$ ),  $p=0.156$ . HFnu showed a non-significant increase from baseline ( $34.66 \pm 20.77$ ) to stimulation ( $40.98 \pm 19.78$ ),  $p=0.156$ , and a non-significant decrease from baseline to post-stimulation ( $28.53 \pm 19.43$ ),  $p=0.096$ . The LF/HF ratio remained stable from baseline ( $2.765 \pm 1.822$ ) to stimulation ( $2.249 \pm 2.125$ ),  $p=0.282$ , but significantly increased post-stimulation ( $4.006 \pm 2.598$ ),  $p=0.014$ . Tragus stimulation: LFnu decreased from baseline ( $64.56 \pm 18.36$ ) to stimulation ( $63.92 \pm 19.53$ ),  $p=0.901$ , but substantially increased post-stimulation ( $73.96 \pm 10.89$ ),  $p=0.022$ . HFnu increased slightly from baseline ( $35.36 \pm 18.34$ ) to stimulation ( $36.01 \pm 19.48$ ),  $p=0.899$ , but significantly decreased post-stimulation ( $25.99 \pm 10.88$ ),  $p=0.022$ . The LF/HF ratio decreased from baseline ( $3.125 \pm 3.176$ ) to stimulation ( $2.364 \pm 1.293$ ),  $p=0.305$ , and showed no significant difference from baseline to post-stimulation ( $3.566 \pm 1.943$ ),  $p=0.456$ .

**Conclusion:** The results of this study suggest that tVNS applied to both the cymba conchae and the tragus elicits similar effects on HRV modulation in healthy individuals.