FACILITATION OF NEUROFUNCTIONAL TRAINING WITH TDCS AND RTMS ON THE LEFT DORSOLATERAL PREFRONTAL CORTEX IN CHILDREN WITH AUTISM SPECTRUM DISORDER: A RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND CLINICAL TRIAL

Giselle Araujo Ferreira[1]
Marcela de Oliveira Araújo[2]
Sara Viana de Abreu Silva[3]
Paula Soares da Silva[4]
Marcele Paganoto Garcia Rodrigues da Silva[5]
Amanda Macedo de Freitas Souza Ramos[6]
Rafael dos Anjos Silva[7]
Caroline Priscila de Oliveira[8]
Luanda André Collange[9]
Claudia Santos Oliveira [10]
Evangelical University of Goiás – UniEVANGÉLICA[1-10]

ABSTRACT

The objective of this study is to compare the effects of ten sessions of neurofunctional training associated with anodal transcranial direct current stimulation (tDCS) or high-frequency repetitive transcranial magnetic stimulation (rTMS) on the left dorsolateral prefrontal cortex in the domain of Participation of the International Classification of Functioning, Disability and Health (ICF) in children with Autism Spectrum Disorder (ASD).in children with Autism Spectrum Disorder (ASD). This is a randomized, placebo-controlled, double-blind clinical trial involving 48 children diagnosed with ASD. The children will be randomly assigned to four groups: tDCS experimental group: neurofunctional training associated with active tDCS; tDCS control group: neurofunctional training associated with placebo tDCS; rTMS experimental group: neurofunctional training performed after active rTMS; and rTMS control group: neurofunctional training performed after placebo rTMS. Participants will be assessed one week before the intervention, one week and one month after the end of the interventions, using the Childhood Autism Rating Scale, Pediatric Assessment of Dysfunction Inventory, and Participation and Environment Measure - Children and Youth. The interventions will consist of five sessions per week, carried out over two consecutive weeks. Neurofunctional training will consist of a circuit of activities (10 minutes) and treadmill training (10 minutes). Neurofunctional training and tDCS application will be performed synchronously for 20 minutes. rTMS will be performed for 20 minutes, with the participant at rest and after the participants have completed the neurofunctional training.

Keywords: autism spectrum disorder, child, participation, transcranial magnetic stimulation, and transcranial direct current stimulation.

Introduction

Noninvasive brain stimulation currently represents a new therapeutic perspective for children with autism spectrum disorder (ASD). The preliminary results available in the scientific literature are encouraging. Facilitating the activity

of the left dorsolateral prefrontal cortex and underlying circuits through anodal transcranial direct current stimulation (tDCS) and high-frequency transcranial magnetic stimulation (rTMS) is resulting in a reduction in important ASD symptoms, such as stereotypical movements, social interaction and communication difficulties, especially when transcranial stimulation is performed in therapeutic programs focused on cognitive-behavioral interventions (LIU *et al.,* 2023).

However, the effects of anodal tDCS and high-frequency rTMS techniques have not been analyzed in children with ASD considering: (1) the facilitation of left dorsolateral prefrontal cortex activity in neurofunctional training programs focused on improving motor skills that may result in greater participation of the child in routine activities and (2) understanding the effects of the two transcranial stimulation techniques, aiming to clarify whether there is superiority of the effects triggered by one of the two techniques in a comparative analysis.

In addition, the International Classification of Functioning, Disability and Health (ICF) is a biopsychosocial model that focuses on interactions between body functions and structures, activities and participation, and contextual factors. Health researchers use the ICF model to report their research results and guide professionals in selecting outcome measures and planning specific interventions for their patients. The literature presents limitations in studies that use this model to report the effectiveness of interventions based on tDCS and rTMS. Most clinical trials present results of interventions on the Activity domain. Participation can be considered under-explored to date, although it is recognized as a key clinical outcome today. Thus, understanding the effects of anodal tDCS and high-frequency rTMS on the Participation domain of the ICF in children with ASD is promising.

Thus, the objective of the project is to compare the effects of ten sessions of neurofunctional training associated with anodal tDCS or high-frequency rTMS on the left dorsolateral prefrontal cortex in the Participation domain of the ICF in children with ASD.

Methodology

This is a randomized, placebo-controlled, double-blind clinical trial involving 48 children diagnosed with ASD, aged between three and eight years, who meet the eligibility criteria.

Participants will be assessed one week before, one week and one month after the end of the intervention, using the Childhood Autism Rating Scale (PEREIRA; RIESGO; WAGNER, 2008), Pediatric Assessment of Dysfunction Inventory (HALEY; COSTER; FAAS, 1991), and Measure of Participation and Environment - Children and Youth (GALVÃO et al., 2018).

The interventions will take place five times a week, over two consecutive weeks, for a total of ten sessions. Participants will be randomly divided into four groups:

- tDCS experimental group: neurofunctional training associated with anodal tDCS on the left dorsolateral prefrontal cortex;
- tDCS control group: neurofunctional training associated with placebo tDCS;
- rTMS experimental group: neurofunctional training performed after high-frequency rTMS on the left dorsolateral prefrontal cortex;
- rTMS control group: neurofunctional training performed after placebo rTMS.

rTMS and tDCS will be applied to the left dorsolateral prefrontal cortex, following the location proposed by the 10-20 electroencephalogram system. Active rTMS will be applied at a high frequency (5Hz). Active rTMS and placebo will be applied for 20 minutes, with the child seated at rest. After rTMS application, participants will undergo neurofunctional training for 20 minutes. r neurofunctional training and tDCS (1mA) will be performed synchronously for 20 minutes. Neurofunctional training will consist of a circuit of activities (10 minutes) and treadmill training (10 minutes). The results will be analyzed statistically assuming a significance level of $p \leq 0.05$.

Expected results

Considering the potential effect of rTMS and anodal tDCS on the left dorsolateral prefrontal cortex, it is expected that the intervention will increase the effect size of neurofunctional training in children with ASD. The study may contribute to understanding whether there are different clinical effects of rTMS and anodal tDCS, as well as demonstrating the superiority of one of the two noninvasive brain stimulation techniques.

Conclusion

The research project schedule involves the start of recruitment and assessment procedures in October 2024. The results obtained will be analyzed and presented in scientific articles.

References

GALVÃO, É. R. V. P.; CAZEIRO, A. P. M.; DE CAMPOS, A. C.; LONGO, E. Measurement of Participation and Environment - Children and Youth (PEM-CY). **Journal of Occupational Therapy of the University of São Paulo,** v. 29, n. 3, p. 237–245, Nov. 30, 2018.

HALEY, S. M.; COSTER, W. J.; FAAS, R. M. A content validity study of the pediatric evaluation of disability inventory. **Pediatric Physical Therapy**, v. 3, n. 4, 1991.

LIU, A.; GONG, C.; WANG, B.; SUN, J.; JIANG, Z. Non-invasive brain stimulation for patients with autism: a systematic review and meta-analysis. **Frontiers in Psychiatry**, v. 14, June 29, 2023.

PEREIRA, A. M.; RIESGO, R. S.; WAGNER, M. B. Childhood autism: Translation and validation of the Childhood Autism Rating Scale for use in Brazil. **Jornal de Pediatria**, v. 84, n. 6, 2008.