PRE-FRONTAL CORTEX NEUROMODULATION BY RTMS AND NEUROFUNCTIONAL TRAINING IN CHILDREN WITH AUTISM SPECTRUM DISORDER: A RANDOMIZED, DOUBLE-BLIND, CONTROLLED CLINICAL TRIAL

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ABSTRACT

The objective of this study is to compare the functional effects of ten sessions of neurofunctional training associated with repetitive transcranial magnetic stimulation (rTMS) on the active left dorsolateral prefrontal cortex and placebo in children with ASD. This is a randomized, placebo-controlled, double-blind clinical trial involving 24 children diagnosed with ASD, aged between three and eight years. The children will be randomly assigned to two groups: Experimental group – neurofunctional training and active rTMS; and Control group – neurofunctional training and 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, Autism Classification System: Social Communication, *timed up and go,* 10-meter walk test, Pediatric Balance Scale, and Participation and Environment Measure - Children and Youth. The interventions will consist of five sessions per week, carried out over two consecutive weeks. rTMS will be applied to the left dorsolateral prefrontal cortex for 20 minutes at a high frequency (5Hz). After rTMS application, participants will undergo neurofunctional training for 20 minutes. Neurofunctional training will consist of a circuit of activities (10 minutes) and gait training on a treadmill (10 minutes). The results will be analyzed statistically assuming a significance level of $p \leq 0.05$.

Keywords: autism spectrum disorder, gait, balance, child, physical therapy, transcranial magnetic stimulation.

Introduction

Noninvasive neuromodulation is gaining increasing prominence in the scientific literature focused on the rehabilitation of children and adolescents. Repetitive transcranial magnetic stimulation (rTMS) is a neuromodulation technique that not only directly targets specific brain areas by increasing their activation, but also modulates areas involved in the entire functional circuitry

connecting different brain regions, thus strengthening the neural network and its functional abilities (ZIEMANN, 2004).

Specifically, studies analyzing the results of rTMS in children and adolescents with Autism Spectrum Disorder (ASD) have shown promising results from stimulation of the left dorsolateral prefrontal cortex, involving a reduction in behavioral symptoms and improvement in communication and social interaction. Currently, advances in science have led to the understanding that rTMS is capable of optimizing the results of behavioral interventions, such as cognitive-behavioral and motor neurofunctional training (LIU *et al.,* 2023).

Although cognitive-behavioral symptoms are a priority in ASD, several motor changes are observed in this population, imposing the worsening of limitations faced in the performance of the most diverse daily activities (REINDAL *et al.*, 2020). However, there is a gap in the literature on the effects of rTMS on the left dorsolateral prefrontal cortex associated with neurofunctional training on motor activities and the participation of children with ASD.

Considering the prospect of optimizing the effect size of motor neurofunctional training, the complexity and intensity of the negative impact of ASD on motor activities and the independence of children, a better understanding of the effects of rTMS in this population is necessary. As it is considered a safe, inexpensive, and easy-to-apply resource, rTMS may contribute positively to the rehabilitation of children with ASD if it is scientifically demonstrated that its neurophysiological effects are capable of promoting the improvement of learning new voluntary motor strategies and postural control.

Thus, the aim of the project is to analyze the effects of ten sessions of neurofunctional training performed after 20 minutes of rTMS application on the active left dorsolateral prefrontal cortex and placebo on the domains of activity (mobility and functional balance) and participation of the International Classification of Functioning, Disability and Health (ICF) in children with ASD.

Methodology

This is a randomized, placebo-controlled, double-blind clinical trial involving 24 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), the Autism Classification System: Social Communication (TAJIK-PARVINCHI *et al.*, 2023), Muscle Strength Assessment, TUG test (*timed up and go (*MARTÍN-DÍAZ *et al.,* 2023), 10-meter walk test (SIVARAJAH *et al.,* 2018), Pediatric Balance Scale (FRANJOINE; GUNTHER; TAYLOR, 2003) and Measure of Participation and Environment - Children and Youth (GALVÃO *et al.,* 2018).

The interventions will consist of five sessions per week, carried out over two consecutive weeks, totaling ten 50-minute sessions. Participants will be randomly divided into two groups: experimental group – neurofunctional training and active rTMS; and control group – neurofunctional training and placebo rTMS. rTMS 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 or sham (placebo) rTMS will be applied for 20 minutes, with the child seated at rest After rTMS application, participants will undergo neurofunctional training for 20 minutes. Neurofunctional training will consist of a circuit of activities (10 minutes) and treadmill gait training (10 minutes). Results will be statistically analyzed assuming a significance level of $p \leq 0.05$.

Expected results

Considering the potential effect of rTMS on the left dorsolateral prefrontal cortex, it is expected that the intervention will increase the effect size of neurofunctional training in children with ASD with only ten intervention sessions. The therapeutic approach studied may represent a paradigm shift in the neurofunctional rehabilitation of children with ASD through an effective, low-cost, and short-term intervention.

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.

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