

**NEUROMODULATION OF THE PRE-FRONTAL CORTEX
BY rTMS AND NEUROFUNCTIONAL TRAINING IN CHILDREN
WITH AUTISM SPECTRUM DISORDER: RANDOMIZED
CONTROLLED DOUBLE-BLIND CLINICAL TRIAL
EUROMODULATION OF THE PRE-FRONTAL CORTEX
THROUGH rTMS AND NEUROFUNCTIONAL TRAINING IN
CHILDREN WITH AUTISM SPECTRUM DISORDER:
RANDOMIZED CONTROLLED DOUBLE-BLIND CLINICAL
TRIAL**

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SUMMARY

The objective of the study project is to compare the functional effects of ten sessions of neurofunctional training associated with repetitive transcranial magnetic stimulation (rTMS) on the active and placebo dorsolateral prefrontal cortex 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 allocated into two groups: Experimental group - neurofunctional training and active rTMS, and Control group - neurofunctional training and placebo rTMS. The participants will be evaluated one week before the intervention, one week and one month after the end of the interventions, using the Childhood Autism Rating Scale, the Autism Classification System: Social Communication, timed up and go, the 10-meter walk test, the Pediatric Balance Scale, and the Participation and Environment Measure for Children and Youth. The interventions will be held five times a 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 the application of rTMS, the participants will undergo neurofunctional training for 20 minutes. The neurofunctional training will consist of an activity circuit (10 minutes) and treadmill gait training (10 minutes). The results will be statistically analyzed assuming a significance level of $p \leq 0.05$.

Keywords: Autism spectrum disorder; gait; balance; child; physiotherapy; transcranial magnetic stimulation.

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Introduction

Non-invasive neuromodulation is gaining increasing prominence in the scientific literature aimed at the rehabilitation of children and adolescents. Repetitive transcranial magnetic stimulation (rTMS) is a neuromodulation resource that not only directly targets specific brain areas by increasing the activation of the activity underlying the stimulation but also involves areas throughout the entire functional circuitry responsible for the connections between brain regions, thereby strengthening the entire 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 the stimulation of the left dorsolateral prefrontal cortex, which involved a reduction in behavioral symptoms and an improvement in communication and social interaction. Currently, advances in science have allowed for the understanding that rTMS is capable of optimizing the results of behavioral interventions, such as, for example, cognitive-behavioral and motor neurofunctional training (LIU et al., 2023).

Although cognitive-behavioral symptoms are a priority in ASD, various motor alterations are observed in this population, exacerbating the limitations faced in performing a wide range of daily activities (REINDAL et al., 2020). However, there is a gap in the literature regarding 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 perspective of optimizing the effect size of motor neurofunctional training, the complexity and intensity of the negative impact of ASD on motor activities and the child's independence, a better understanding of the effects of rTMS on this population is necessary. As it is considered a safe, inexpensive, and easy-to-apply resource, rTMS could positively contribute 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 objective of the project is to analyze the effects of ten sessions of neurofunctional training conducted after 20 minutes of active and placebo rTMS application on the left dorsolateral prefrontal cortex on the activity (mobility and functional balance) and participation domains 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.

The participants will be evaluated one week before, one week after, and one month after the end of the intervention, using the Childhood Autism Rating Scale (PEREIRA; RIESGO; WAGNER, 2008), Autism Classification System: Social Communication (TAJIK-PARVINCHI et al., 2023), Muscle Strength Assessment, 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 Participation and Environment Measure - Children and Youth (GALVÃO et al., 2018).

The interventions will occur five times a week, carried out over two consecutive weeks, totaling ten sessions of 50 minutes each. The participants will be randomly assigned to 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 with high frequency (5Hz). The application of active and placebo rTMS will be carried out for 20 minutes, with the child sitting at rest. After the application of rTMS, the participants will undergo neurofunctional training for 20 minutes. The neurofunctional training will consist of an

activity circuit (10 minutes) and treadmill walking training (10 minutes). The 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 enhance the effect size of neurofunctional training in children with ASD, with just ten intervention sessions. The therapeutic approach studied could represent a paradigm shift in the neurofunctional rehabilitation of children with ASD, through an effective, low-cost, and short-duration intervention.

Conclusion

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

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