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A network meta-analysis of non-invasive brain stimulation interventions for autism: evidence from randomized controlled trials

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ADMINISTRATIVE INFORMATION

Support - Currently none.

Review Stage at time of this submission - Formal screening of search results against eligibility criteria.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202370003

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 01 July 2023 and was last updated on 01 July 2023.

INTRODUCTION

Review question / Objective PICOS criteria: (1) Patient: participants with a diagnosis of autism spectrum disorder; (2) Intervention: any non-invasive brain stimulation; (3) Comparison: sham, active, or waitlist controls; (4) Outcome: changes in overall core symptoms, social difficulties, and repetitive or restricted behaviors, and dropout rates and serious adverse events; and (5) Study design: randomized controlled trials.

Condition being studied Autism spectrum disorder is a developmental disorder that affects communication, social interaction, and behavior. Individuals with autism spectrum disorder may experience challenges in social interaction, such as difficulty with nonverbal communication cues, developing and maintaining relationships, and understanding social norms. They may also exhibit repetitive behaviors, restricted interests, and sensory sensitivities.

In the context of autism spectrum disorder, non-invasive brain stimulation is still an area of ongoing research, and its effectiveness as a standalone treatment for core autism spectrum disorder symptoms is not yet well-established. However, some studies have shown promising results in improving certain aspects of autism spectrum disorder, such as social cognition, repetitive behaviors, and executive function.

METHODS

Participant or population Participants with a diagnosis of autism spectrum disorder.

Intervention Any non-invasive brain stimulation interventions.

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Comparator Sham, active, or waitlist controls.

Study designs to be included Randomized controlled trial.

Eligibility criteria The criteria for inclusion were: (1) studies involving human participants; (2) participants diagnosed with autism based on a valid method (i.e. using the Diagnostic and Statistical Manual of Mental Disorders, International Classification of Diseases, or diagnosis by a certified specialist5) (3) studies providing both pre- and post-intervention scores or score changes regarding overall autism core symptoms using an autism assessment scale such as the Social Responsiveness Scale (SRS); (4) RCTs that utilized either sham, active, or waitlist controls and employed either a crossover or parallel study design. Conversely, studies were excluded based on the following criteria: (1) those not reporting the outcome of interest (overall autism core symptom score); (2) case series or reports, conference papers, protocols, and non-peer-reviewed articlesThe criteria for inclusion were: (1) studies involving human participants; (2) participants diagnosed with ASD based on a valid method (i.e. using the Diagnostic and Statistical Manual of Mental Disorders, International Classification of Diseases, or diagnosis by a certified specialist5) (3) studies providing both pre- and post-intervention scores or score changes regarding overall ASD core symptoms using an ASD assessment scale such as the Social Responsiveness Scale (SRS);6 (4) RCTs that utilized either sham, active, or waitlist controls and employed either a crossover or parallel study design. Conversely, studies were excluded based on the following criteria: (1) those not reporting the outcome of interest (overall ASD core symptom score); (2) case series or reports, conference papers, protocols, and non-peer-reviewed articles.

Information sources PubMed, Embase, Cochrane CENTRAL, and other gray literature databases.

Main outcome(s) Two primary outcomes were examined in this study, including efficacy and acceptability. Efficacy expressed as change in assessment score of ASD overall core symptoms after NIBS intervention. We accepted a wide range of validated rating scales for overall core symptoms (e.g. SRS, Childhood Autism Rating Scale [CARS], Autistic Behavior Checklist [ABC], Autism Treatment Evaluation Checklist [ATEC], Ritvo Autism Asperger Diagnostic Scale [RAADS], Gilliam Autism Rating Scale [GARS-2], and Autism Spectrum Quotient [AQ]) since no optimal outcome measure is used universally. Acceptability was expressed as dropout rate, which was defined as percentage of patients who discontinued the study for any reason before study completion.

Additional outcome(s) We assessed the following secondary outcomes: (1) treatment efficacy for social symptoms; (2) treatment efficacy for behaviors; and (3) serious adverse events (e.g. seizure, suicidal ideation, or auditory injuries).

Quality assessment / Risk of bias analysis The risk of bias of each included trial using the Cochrane risk of bias tool version 2.

Strategy of data synthesis We conducted network meta-analysis to assess the pre-post changes for overall, social, and behavior symptoms (continuous variables) and incidence rates for dropout rate (categorical variables) of the aforementioned outcomes. We estimated standardized mean differences with 95% confidence intervals for continuous variables and odds ratios and 95% confidence intervals for categorical variables.

Subgroup analysis No.

Sensitivity analysis we conducted a sensitivity analysis for only pediatric and adolescent participants (i.e. excluding studies which included patients > 18 years old).

Language restriction No.

Country(ies) involved Taiwan.

Keywords efficacy, safety, autism, non-invasive brain stimulation.

Contributions of each author

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