INPLASY PROTOCOL

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No conflicts of interest to declare.

Altering the Gut Microbiome to Modulate Behavior Manifestations in Autism Spectrum Disorders: A Systematic Review

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Review question / Objective: How do probiotics, prebiotics, and antibiotics influence the gut-brain axis to therapeutically modulate the behavioral manifestations of autism spectrum disorders.

Condition being studied: Autism spectrum disorders.

Main outcome(s): Main outcomes sought will include behavioral manifestations of autism spectrum disorders as measured by validated questionnaires like ATEC, GSI, Autism-spectrum quotient, as well as measures of specific symptoms like constipation and frequency of bowel movements.

INTRODUCTION

Review question / Objective: How do probiotics, prebiotics, and antibiotics influence the gut-brain axis to therapeutically modulate the behavioral manifestations of autism spectrum disorders.

Rationale: Dysfunction along the gut-brain axis is increasingly implicated in the pathogenesis of autism spectrum disorders (ASD). In addition to its

neurodevelopmental deficits, ASD is also characterized by a range of gastrointestinal symptoms, which increase in proportion to the severity of ASD. Moreover, many studies have found that those with ASD have an altered intestinal microbiome composition. Current evidence appears inconsistent, therefore we aim to conduct a review to analyze this.

Condition being studied: Autism spectrum disorders.

METHODS

Search strategy: For this systematic review, PubMed will be used as the primary database to search for relevant studies conducted in previous years. Three separate searches will be performed and subsequently combined using a 10-year and human only filter and the following MeSH terms: ("Anti-Bacterial Agents"[Pharmacological Action] AND "Autism Spectrum Disorder"[Mesh]), ("Dietary Fiber"[Mesh] AND "Autism Spectrum Disorder"[Mesh]), ("Fecal Microbiota Transplantation"[Mesh] AND "Autism Spectrum Disorder"[Mesh]) and ("Probiotics"[Mesh] OR "Synbiotics"[Mesh]) OR "Fecal Microbiota Transplantation"[Mesh] AND "Autism Spectrum Disorder"[Mesh]). Studies will also be identified from the researchers' knowledge of the field. These studies will then assessed for eligibility, depublicated, and screened based on title and abstract relevance to the research question. After screening, a whole-text analysis will be performed to fully evaluate the appropriateness of the studies for the research question. Finally, after identification and screening, these studies will be analyzed using the Cochrane Risk of Bias (RoB) tool to evaluate their strength.

Participant or population: Children with Autism spectrum disorders.

Intervention: Probiotic, prebiotic and antibiotic supplementation.

Comparator: Behavioral manifestations of ASD, e.g. ATEC and GSI questionnaire.

Study designs to be included: RCTs, open-label trials, crossover studies, observational studies, prospective cohort, and retrospective cohort studies

Eligibility criteria: Screened based on title and abstract relevance to the research question. After screening, a whole-text analysis will be performed to fully evaluate the appropriateness of the studies for the research question. Key criteria for eligibility will include availability of ASD outcome measurements and probiotic/prebiotic/antibiotic intervention or use.

Information sources: PubMed MeSH search and via authors own knowledge of the field.

Main outcome(s): Main outcomes sought will include behavioral manifestations of autism spectrum disorders as measured by validated questionnaires like ATEC, GSI, Autism-spectrum quotient, as well as measures of specific symptoms like constipation and frequency of bowel movements.

Data management: COVIDENCE will be used to manage and track data.

Quality assessment / Risk of bias analysis: Quality assessment and risk of bias will be performed via the Cochrane RoB tool for RCTs and non-RCTs.

Strategy of data synthesis: A systematic narrative synthesis will be presented in the text to summarize and explain the findings and characteristics of the included studies. Studies will be qualitatively analyzed, compared, and discussed based on the strength of their study design and risk of bias.

Subgroup analysis: Qualitative analysis only.

Sensibility analysis: Qualitative analysis only.

Language: English only.

Country(ies) involved: USA.

Contributions of each author:
Author 1 - Camron Davies - Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data Curation, Writing Original Draft, Writing - Reviewing and Editing, Visualization.
Author 2 - Dibyanshi Mishra - Data Curation, Writing Original Draft, Writing - Reviewing and Editing.
Author 3 - Rebecca S. Eshraghi - Conceptualization, Writing - Reviewing and Editing.
Author 4 - Jeenu Mittal - Writing - Reviewing and Editing.
Author 5 - Rahul Sinha - Investigation, Data Curation, Writing - Reviewing and Editing.
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