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Decoding SCN2A Variants: Bridging Genetics and Phenotypes in Autism Spectrum Disorder

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ADMINISTRATIVE INFORMATION

Support - N/A.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 5 February 2025 and was last updated on 5 February 2025.

INTRODUCTION

Review question / Objective This systematic review investigates the relationship between SCN2A mutations and ASD phenotypes.

Condition being studied Autism Spectrum Disorder (ASD).

METHODS

Participant or population Patient with ASD.

Intervention Not applicable.

Comparator Not applicable.

Study designs to be included Case Series, Cohort, Randomized Controlled Trials, Cross-sectional.

Eligibility criteria ASD diagnosis.

Information sources The search was conducted using electronic databases, including PubMed, Embase, Web of Science, SCOPUS, and ScienceDirect.

Main outcome(s) Extracted data included patient demographics (age, sex), the presence or absence of an ASD diagnosis, genetic variations, and association statistics (such as p-values) quantifying the correlation between SCN2A mutations and ASD.

Quality assessment / Risk of bias analysis The risk of bias was assessed using the Joanna Briggs Institute (JBI) critical appraisal checklist, tailored to the study type[46-49]. The GRADE criteria and the Risk of Bias Assessment tool for Non-Randomized Studies (RoBANS) were also applied to formally assess the quality of evidence and potential bias in the included studies. Three researchers critically

reviewed the included studies for scientific quality and control of confounders.

Strategy of data synthesis Data from studies that met the inclusion criteria were synthesized and presented in both tabular and narrative formats. The characteristics, methods, outcomes, and study quality (RoB) were described. Data were reported as medians, percentages, ranges, and means with standard deviations, where applicable. Subgroup analyses were performed based on sex (male vs. female) and age groups to explore any differential effects of SCN2A mutations in these populations.

Subgroup analysis N/A.

Sensitivity analysis N/A.

Country(ies) involved USA.

Keywords Autism Spectrum Disorder; SCN2A; Nav1.2 sodium channel; genetic mutations; neurodevelopmental disorders; genotype-phenotype correlation; de novo mutations; personalized medicine; intellectual disability.

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