

Title: Integrating Biomarkers into Polygenic Risk Models for Autism

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Abstract

Autism is a multivariate neurodevelopmental condition with high heritability (80 – 90%). Polygenic risk scores (PRS) offer a potential tool to further explore the genetic background of multivariate conditions, such as autism. Due to the weak predictive power of conventional PRS, models integrating additional biomarkers could be used to improve prediction performance and interpretability.

The aim of the work is to explore the existing polygenic risk score for autism and attempt to improve upon it by introducing additional biomarkers, such as microbiome data, gene set enrichment data and known autism associated genes from the Simons Foundation Autism Research Initiative (SFARI) database. The data used includes 169 whole genome sequencing samples from the Genome, Environment, Microbiome and Metabolome in Autism (GEMMA) study cohort. Baseline PRS were calculated using the largest genome-wide association study (GWAS) for autism to date (Grove et al., 2019). Subsequent models were then further constructed and tested by integrating additional biomarkers.

The baseline PRS showed moderate though non-significant associations with autism status. While including microbiome markers did not enhance the model, minor improvements to the model predictiveness could be seen when adjusting the weights using SFARI gene scores or including enriched immune gene-set information, although the associations remained non-significant. The results suggest that while integrating biomarkers could be used to refine the PRS, capturing the biological complexity of autism in the future would require larger cohorts with more comprehensive multi-omics integration.