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TITLE: Integrative multi-omics analysis of genomic, epigenomic, and metabolomic data for childhood aggressive behavior

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ABSTRACT:

Multi-omics studies allow for identification biomarkers for improved patient stratification

for diagnosis and treatment, and elucidation of underlying disease-associated biological processes. In this project we perform an integrated multi-omics analysis for childhood aggression based on genomics, epigenomics and metabolomics data. First-morning urine and buccal-cell samples were collected in a cohort of twin pairs ($N = 798$ [365 complete pairs], mean age = 9.5 [SD = 1.9], male = 52%), recruited from the Netherlands Twin Register (NTR), to assess urinary metabolites, buccal methylation markers and genotypes. Genotype information is available from twins and their parents and is used to obtain transmitted and non-transmitted polygenic scores for aggression and correlated traits. First, using 20% of the dataset, the discriminative capability of each omics level is assessed with Partial Least Squares Discriminant Analysis (PLS-DA); and potential pairwise cross-omics relationships are highlighted with PLS. Next, based on these results, we apply a multi-block PLS-DA (DIABLO) in a training set of 50% of the data to combine all omics levels in an integrated multi-omics analysis. Third, the method allows us to predict aggression status in the final 30% of the dataset and assess its performance. This model will be validated in an independent sample of children referred to a youth psychiatry clinic (Curium-LUMC, the Netherlands; $N = 162$, mean age = 10.2 [SD = 1.8], male = 74.1%). Multi-omics analysis will provide insight in the underlying biological processes of childhood aggressive behavior which may be used to find new drug targets in the future.

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