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Association between urokinase receptor gene *PLAUR* polymorphisms and negative symptom subdomains in schizophrenia

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Negative symptoms in schizophrenia – particularly avolition/apathy (AA) and diminished expression (DE) – are linked to disability and poor treatment response. Recent findings suggest involvement of neuroinflammatory pathways. The urokinase plasminogen activator receptor (uPAR), encoded by *PLAUR*, modulates neuroinflammation, neurodevelopment, and extracellular matrix remodeling–processes relevant to schizophrenia and sensitive to perinatal insults. We hypothesized that *PLAUR* polymorphisms influence negative symptoms and interact with early-life risk factors.

We examined 552 schizophrenia-spectrum patients (64.7% women, mean age 35.7 ± 12.8 years, illness duration 11.6 ± 10.3 years). Inclusion criteria: ICD-10 F20.x/F25.x, age ≥16, European ancestry, PANSS data. PANSS scores were used to quantify symptom domains. Premature birth and birth complications were identified from medical records.

Genotyping of *PLAUR* SNPs (rs4760, rs344781, rs344779) was based on Illumina GSA v3 array data, processed in PLINK. Statistical analyses used JASP v0.19.0. Hardy–Weinberg equilibrium was tested via χ^2. ANCOVA assessed SNP and environmental effects on PANSS domains, with sex and illness duration as covariates; Tukey's HSD was used for post-hoc comparisons.

SNP rs4760 was associated with total negative symptoms ($p = 0.002$), AA ($p = 0.005$), and DE ($p = 0.002$). AA genotype carriers had lower scores than G+ (Mean Diff = –2.163, $p = 0.002$). This remained significant only in patients without perinatal adversity. rs344781 showed a main effect on negative symptoms ($p = 0.016$) and interacted with prematurity (SA $p = 0.014$, DE $p = 0.009$); TT carriers born preterm had lower DE scores ($p = 0.048$). rs344779 was associated with positive ($p = 0.016$) and general symptoms ($p = 0.026$), and showed a trend-level interaction with prematurity in the SA domain ($p = 0.041$).

Our results highlight the contribution of *PLAUR* polymorphisms, especially rs4760 and rs344781, to negative symptom dimensions in schizophrenia, potentially mediated by neuroinflammation and gene–environment interactions.

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