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THE EFFECT OF DTNBP1 AND COMT RISK VARIANTS AND COMORBID DRUG-ABUSE IN PATIENTS WITH SCHIZOPHRENIA: A GENE-ENVIRONMENT INTERACTION?

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Introduction: Earlier studies have shown that candidate gene risk polymorphisms and psychoactive substance abuse influence the frequency and severity of psychosis.

Objectives: In this study we examined whether the most studied schizophrenia risk polymorphisms and psychoactive substance abuse interact in their influence on symptom severity and neurocognition.

Methods: We analyzed the clinical data of 280 schizophrenia patients, including genotyping data of the candidate genes NRG1, DTNBP1, RGS4, G72/G30 and PIP5K2A. Patients were assessed clinically by the Positive and Negative Symptom Scale (PANSS) and information about substance abuse was based on self-report and reviewing patient charts. We tested for possible interactional effects using the General Linear Model (GLM) analysis.

Results: 15,8% of patients reported episodic or regular substance abuse, the vast majority (92%) used cannabis or the combination of cannabis and another drug. Substance abuse was associated with higher scores of the PANSS hostility/excitement factor, independent of sex, age, or genetic results ($F=4,02;p=0,04$). We found significant interactional effects of the DTNBP1 gene risk polymorphisms and substance abuse on different PANSS factors: rs2619528 and positive substance abuse interaction were associated with higher scores on the PANSS negative factor ($F=4,6;p=0,03$), and the PANSS depression factor ($F=4,75;p=0,03$). Moreover the rs3213207 - substance abuse interaction was associated with higher scores on the PANSS cognitive factor ($F=7,55;p=0,006$). Carriers of the Val allele of the COMT Val158Met polymorphism demonstrated significantly higher scores on the PANSS depression factor ($F=5,53;p=0,02$).

Conclusions: Our results underscore the importance of gene-environment interactions in the phenotypic heterogeneity of schizophrenia.