M44. INVESTIGATION OF GENETIC VARIANTS WITHIN GENES TARGETS OF ANTIPSYCHOTIC RESPONSE AND THEIR SIGNAL CASCADE IN SCHIZOPHRENIA AND ANTIPSYCHOTIC RESPONSE

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Background Schizophrenia (SCZ) is a devastating psychiatric disease that affects about 1% of the population and ranks among the top 10 causes of disability worldwide. Although environmental factors can play a relevant role in the development of SCZ, evidences from family, twin, and adoption studies suggest a strong genetic component in the etiology of the disease. Similarly, a genetic contribution for antipsychotic outcome has been suggested. In the present study we investigated the associations among two distinct groups of single nucleotide polymorphisms (SNPs) within 1) genes coding for molecular targets of antipsychotic drugs and 2) genes whose products were involved with the signal transduction of the primary molecular targets.

Methods Two independent samples were investigated in this study. A Korean sample of 176 in-patients and 326 healthy controls and an Italian sample of 83 patients and 195 healthy controls. A total of 100 SNPs within 18 genes were analyzed in the two samples. We investigated 1) differences among genotypic and allelic frequencies in patients with SCZ compared with healthy control subjects and 2) possible influence of the SNPs under investigation on clinical improvement, as measured with the PANSS total scale in SCZ patients.

Results In the Italian sample, rs12668837 within NCAPG2 and rs7439 within PKDCC showed a different allelic distribution between cases and controls. In the pharmacogenetic analysis, variants within CHRNA7, MAPK1 genes (which coding for antipsychotic targets) and variants within PLA2G4A, ESYT2 and HOMER1 genes (which are involved in the antipsychotic targets signal transduction) showed trends of association with antipsychotic response as measured by PANSS scale.

Discussion Overall, our data suggest a possible role of these two groups of genes in both SCZ pathophysiology and antipsychotic response. A limited sample size and the consequent risk of false positive findings should be carefully taken into consideration when evaluating these results.

Disclosure: Nothing to Disclose.