

S28-04 - PHARMACOGENETICS OF EXTRAPYRAMIDAL MOTOR SIDE EFFECTS IN THE TREATMENT OF SCHIZOPHRENIA

R. Musil¹, D. Rujescu², I. Spellmann¹, A. Mayr³, P. Zill⁴, I. Giegling², B. Bondy⁴, N. Müller¹, H.-J. Möller⁵, M. Riedel¹

¹Psychopharmacology, ²Molecular and Clinical Neurobiology, ³Medical Statistics, ⁴Pharmacogenetics, ⁵Clinic for Psychiatry and Psychotherapy of LMU University of Munich, Munich, Germany

Introduction: Since the introduction of second generation antipsychotics (SGA) extrapyramidal-motor symptoms (EPS) have become a lesser problem in the treatment of schizophrenic patients. Yet, some SGAs display these adverse events and first generation antipsychotics are still widely used. Several genetic polymorphisms have been found to be associated with the occurrence of EPS.

Objectives: In this study we tried to identify genes related to EPS from an animal model and then replicated the findings in schizophrenic patients.

Aims: To identify new genes and show their relevance in the treatment of schizophrenic patients.

Methods: Rats were treated with haloperidol or saline and differential gene expression was assessed by using microarrays. We genotyped 285 schizophrenic patients for candidate genes and differentially expressed genes derived from the animal model. All patients were treated monotherapeutically with different antipsychotics within randomized controlled trials. EPS were assessed weekly using the ESRS and BAS. We used a linear model (ANCOVA) with PANSS total at baseline, type of medication and premedication as covariates for all investigated SNP's.

Results: We found several SNPs to be associated with the occurrence of EPS. The best results were obtained for SNPs within the genes of Phospholipase C epsilon 1 (PLCe1), Methionine Sulfoxide Reductase B3 (MSRB3), Chloride Intracellular Channel 6 (CLIC6), Prolactin Receptor (PRLR) and Dopamine Receptor D4 (DRD4). Effect sizes were between 1.7 and 4.9.

Conclusions: We could replicate some findings of the literature and identified four new genes possibly related to EPS. Some of these genes were recently related to schizophrenia.