

P03-124

GABRB2 IN SCHIZOPHRENIA AND BIPOLAR DISORDER: DISEASE ASSOCIATION, GENE EXPRESSION AND CLINICAL CORRELATIONS

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Aims: Previously the GABA(A) receptor beta-2 subunit gene GABRB2 was found to be associated with schizophrenia (SCZ). For SNPs and haplotypes in GRBR2, the associations with bipolar disorder (BPD), the functional consequences on GABRB2 expression and their relationship to demographic and clinical characteristics in BPD and SCZ remain to be elucidated.

Method: Case-control analysis was performed for association study of GABRB2 with BPD, and its mRNA expression in postmortem BPD brains was examined using quantitative real-time PCR. Quantitative trait analysis was subsequently employed to assess the covariate effects of demographic and clinical characteristics on genotypic correlation of GABRB2 expression in SCZ and BPD.

Results: Significant association of GABRB2 with BPD and reduction in GABRB2 mRNA expression in BPD brains were observed in the present study. Duration of illness (DOI) was found to be a significant covariate for the correlation of the disease-associated SNPs rs1816071, rs1816072 and rs187269 with GABRB2 expression in both SCZ and BPD. For individuals with homozygous major genotypes of these SNPs, while GABRB2 expression increased with age in the controls, it decreased with DOI and age in SCZ, and with DOI in BPD. With age of onset as covariate, these three SNPs were significantly correlated with antipsychotic dosage in SCZ.

Conclusion: These results have thus revealed correlations of GABRB2 SNPs and expression not only with the occurrence of SCZ and BPD, but also with the clinical characteristics of patients, therefore providing support for a shared etiological role played by the gene in both diseases.