

GWAS による強迫性障害のセロトニン再取り込み阻害薬治療および抗精神病薬付加療法への治療反応性と関連するパスウェイの同定

Calcium Signaling Pathway Is Associated with the Long-Term Clinical Response to Selective Serotonin Reuptake Inhibitors (SSRI) and SSRI with Antipsychotics in Patients with Obsessive-Compulsive Disorder

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【Object】 Obsessive-compulsive disorder (OCD) is a neuropsychiatric disorder with a prevalence of approximately 2%. Selective serotonin reuptake inhibitors (SSRI) are well-established first-line pharmacological treatments for OCD, and antipsychotics are used as an augmentation strategy for SSRI in SSRI-resistant patients with OCD. The purpose of the present study is to identify genetic variants and pathways which are associated with the long-term clinical response to SSRI or SSRI with antipsychotics in OCD.

【Methods】 We performed a genome-wide association study in 96 OCD patients. Clinical symptoms were evaluated at baseline and at the end of treatment using the Yale Brown Obsessive-Compulsive Scale (Y-BOCS). To evaluate the effect of each SNP on the clinical response to a SSRI or a SSRI with antipsychotics, a logistic regression analysis was performed using the PLINK software with adjustment for covariates sex, age, onset age and Y-BOCS baseline score. Next we conducted pathway-based analyses by using Improved Gene Set Enrichment Analysis for Genome-wide Association Study (i-GSEA4GWAS) to examine the combined effects of genetic variants on the clinical response in OCD.

【Results】 We didn't reveal any genetic variants associated with clinical responses to SSRI or SSRI with an atypical antipsychotic at genome-wide significance. However, we identified 8 enriched pathways in the SSRI treatment response and 5 enriched pathways in the treatment response to SSRI with an antipsychotic medication (FDR < 0.05). Notably, the calcium signaling pathway was identified in both treatment responses.

【Conclusion】 Our results may provide the clues of the mechanisms of treatment response in OCD.