P-1104 - THE EFFECT OF CLOZAPINE ON THE EXPRESSION OF OBESITY GENES

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Clozapine is a second generation antipsychotic drug that is often used for treatment of schizophrenia. Although clozapine does not produce extrapyramidal side effects, it is well documented that it often causes a substantial increase in body weight among the patients who have received the treatment. This is a major issue in antipsychotic medication of schizophrenia as obesity is a risk factor for the development of type II diabetes, cardiovascular disease and certain types of cancer. The molecular mechanism that underlies this off-targeting effect has been poorly understood, but we hypothesize that the genes involved in obesity may play a role in developing clozapine-induced obesity. In this study, accordingly, we applied a human cell line (U937 cells) with quantitative PCR analysis to examine the effect of clozapine on the expression of obesity genes that were identified by genome-wide association study (GWAS). Our results revealed that expression of the neuronal growth regulator 1 (*NEGR1*) gene was significantly higher in U937 cells treated with clozapine concentrations of 0.5µg/ml (P=0.0165) and 1.0µg/ml (P=0.021), respectively, as compared with that in the vehicle-treated cells. This initial finding suggests that *NEGR1* may be a target of clozapine, leading to the development of drug-induced obesity. The *NEGR1* gene will be further investigated to determine its association with schizophrenia and to clarify what mechanism may be involved in its expression.

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