統合失調症患者における酸化ストレス関連遺伝子の遺伝子多型と代謝異常の関係

Association between oxidative stress-related genes polymorphisms and metabolic abnormalities among schizophrenia patients

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Schizophrenia patients are at an increased risk of obesity and metabolic abnormalities, which are strongly associated with the development of metabolic diseases including cardiovascular diseases in comparison with general populations. Since oxidative stress contributes to the metabolic abnormalities, we investigated or not whether the oxidative stress-related genes polymorphisms affected the risk for metabolic abnormalities among schizophrenia patients. The present cross-sectional study was conducted among 256 schizophrenia patients (147 males and 109 females, mean age: 51.6 ± 14.7 years) and 194 age-matched controls (110 males and 84 females, mean age: 52.2 ± 9.0 years). The effects of the polymorphisms of methylenetetrahydrofolate reductase (MTHFR) rs1801133 (C677T), rs1801131 (A1298C), glutathione S-transferase (GST)T1 null, GSTM1 null and GSTK1 rs1917760 (G-1308T) on the prevalence of overweight (body mass index >=25 kg/m^2) and components of metabolic syndrome (i.e. waist circumstance >=90 cm in males or >=80 cm in females, systolic blood pressure >=135 mmHg or diastolic blood pressure >=85 mmHg, fasting blood glucose >=100 mg/dl, triglyceride >=150 mg/dl and high-density lipoprotein cholesterol <40 mg/dl in males or <50 mg/dl in females) by structural equation modeling. Among the female schizophrenia patients, the MTHFR rs1801133 T/T genotype increased the risk of overweight (P <0.05), and this genotype effect was associated with a risk of metabolic abnormalities (P <0.05). Furthermore, the MTHFR rs1801133 T/T genotype increased the risk of overweight (P <0.05), thus affecting the risk of metabolic abnormalities (P <0.05) in schizophrenia patients with current-smoking status. The effects of GSTK1 T allele and GSTM1 null genotype on the increased risk of overweight were confirmed in the male schizophrenia patients and/or the patients with current-smoking status (P <0.05). In contrast, no association between the polymorphisms and risk of metabolic abnormalities was observed in control subjects. In conclusion, these results suggest that the oxidative stress-related genes polymorphisms (i.e. MTHFR rs1801133, GSTK1 rs1917760 and GSTM1 null) may be a significant risk factor for overweight-related metabolic abnormalities among schizophrenia patients in relation to gender differences and/or smoking status. This information may aid in the genetic-based prevention of overweight and metabolic abnormalities in the schizophrenia patients.