Sex-specific interaction between MAOA promoter polymorphism and Apo ε2 allele in major depressive disorder in the Chinese population
Chi-Hung Lin¹,², Yong-Yuan Chang³ and For-Wey Lung⁴,⁵,⁶

Major depressive disorder (MDD) is one of the most common psychiatric illnesses, and causes considerable impairment in social functioning, employment, and physical ability. An earlier study showed the excessive high-activity long alleles of the MAOA promoter polymorphism that result in elevated MAOA activity, which are risk factors for MDD-related suicide (Du et al., 2002). Fan et al. (2006) further showed that the Apo ε2 allelic frequency in patients with MDD was significantly lower than that in healthy controls, leading to the conclusion that the Apo ε2 allele likely provides a protective effect against MDD in the Chinese population. The aim of this study was to investigate the potential role between MAOA promoter and ApoE polymorphism simultaneously in MDD.

There were 253 patients diagnosed with MDD, 91 men and 162 women, with a mean age of 44.48 years (SD = 15.17) and 411 randomly selected community controls, 178 men and 233 women, with a mean age of 45.32 years (SD = 13.85).

Both ApoE and MAOA promoter polymorphism among the patients and controls were in the Hardy–Weinberg equilibrium. Logistic regression results showed that MDD was associated with MAOA genotypes [P = 0.039, odds ratio (OR) = 1.476, 95% confidence interval (CI) = 1.019–2.137] when adjusting for sex (P = 0.018, OR = 1.508, 95% CI = 1.074–2.118), and more statistically significant with MAOA genotypes (P = 0.017, OR = 1.591, 95% CI = 1.085–2.331) when adjusting for sex (P = 0.016, OR = 1.535, 95% CI = 1.084–2.172) and Apo ε2 (P < 0.001, OR = 0.050, 95% CI = 0.012–0.208). The effect of MAOA promoter polymorphism (P = 0.005, OR = 5.659, 95% CI = 1.708–18.752) was more associated with MDD when adjusting for MAOA genotype–sex interaction (P = 0.028, OR = 0.422, 95% CI = 0.195–0.912). In addition, the analysis of the estimated relative risks of MAOA genotype variation (high-activity genotype/low-activity genotype) in relation to sex in patients with MDD and the controls showed that in male participants with high-activity MAOA genotypes, there was 5.986 times on the risk of contributing vulnerability to MDD, compared with the female controls (OR = 0.981).

Population structure influences even carefully designed studies and can result in the spurious association of alleles with disease genes or phenotypes (Helgason et al., 2005). Different populations have exhibited different distribution frequencies of the ApoE and MAOA promoter polymorphism, which may have led to false-negative or false-positive evidence against association. Hence, both the ApoE genotypes and MAOA genotypes of participants in this study were in the Hardy–Weinberg equilibrium for a suitable parametric estimate.

Gene–gene interaction is commonly found in human diseases, and the single polymorphisms typically do not replicate across independent samples (Moore, 2003). The Apo ε2 allele was not only a protective factor for MDD, but also a potential confounding covariate for the MAOA promoter polymorphism in MDD. The OR of sex-specific genotype relative risks estimation further showed that we should evaluate the gene–sex interaction effects on human MDD, while taking into account individual heterogeneity in the genetic and nongenetic factors in future studies.

References