Effects of Interaction Between Dopamine D2 Receptor and Monoamine Oxidase A Genes on Smoking Status in Young Men

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Abstract
Although the effect of gene–gene interaction on nicotine–dopamine metabolism for smoking behavior has been reported, polymorphisms of dopamine D2 receptor (DRD2) and monoamine oxidase A (MAOA) have not been simultaneously examined among smokers. In this study, 481 young Taiwanese men completed a self-report questionnaire on smoking status, and data were obtained on polymorphisms of DRD2 rs1800497, DRD2 rs1079597, MAOA rs309850, and MAOA rs1137070, urinary nicotine, and urinary cotinine. In a comparison of 261 current smokers and 220 never smokers, odds ratios (ORs) for the development of smoking in all genotypes were not statistically significant. Among smokers with DRD2 rs1079597 GG/MAOA rs309850 3-repeat, the OR of heavier smoking was 2.67 times higher (95% confidence interval [CI]: [1.08, 6.59], \( p = .031 \)) and the score on the Fagerstrom test for nicotine dependence was higher (4.26 vs. 2.83) than in those with DRD2 rs1079597 AA/MAOA rs309850 3-repeat. Adjusted urinary cotinine concentration was significantly different between those two groups (median value: 95.83 ng/\( \mu \)l vs. 133.24 ng/\( \mu \)l, respectively, \( p = .045 \)). These findings suggest that the interaction of DRD2 rs1079597 and MAOA rs309850 3-repeat affects smoking intensity in young Taiwanese men.

Keywords
dopamine D2 receptor, monoamine oxidase A, smoking intensity

Tobacco smoking is a global health problem and Taiwan is no exception (Health Promotion Administration, 2013). Nicotine is the major psychoactive ingredient in tobacco (Henningfield, Cohen, & Pickworth, 1993). The addictive nature of nicotine is multifactorial, involving both environmental and genetic factors (Agrawal et al., 2012; Caron, Karkazis, Raffin, Swan, & Koenig, 2005). The interaction between nicotine and dopamine should be considered when exploring these genetic factors. Nicotine activates dopaminergic neurons and enhances dopamine release, which leads to feelings of pleasure and reward (Fowler & Kenny, 2014).

Of the genetic variants associated with smoking, one of the most widely studied is the dopamine D2 receptor (DRD2) polymorphism. In particular, researchers have increasingly studied DRD2 rs1800497 (DRD2 TaqI A) and DRD2 rs1079597 (DRD2 TaqI B) in this context (Ohmoto et al., 2013; Spitz et al., 1998). DRD2 is localized in chromosome 11 q22-q23. The C-to-T transition of the DRD2 rs1800497 polymorphism causes an amino acid change (Glu713Lys), which seems to significantly reduce the specificity of receptor binding (Vereczkei et al., 2013). The A-to-G substitution of DRD2 rs1079597 may alter DRD2 density in the striatum (Suriyaprom, Tungrongchitr, & Harroongroj, 2013). Investigators have been studying the monoamine oxidase A (MAOA) gene, located in the short arm of the X chromosome in relation to smoking behavior since 2005 (S. Huang et al., 2005). In particular, researchers have typically focused on two polymorphisms of MAOA: MAOA rs309850, a variable number tandem repeat polymorphism, and MAOA rs1137070 (MAOA-LPR), an EcoRV polymorphism (Jin et al., 2006). Researchers have reported that MAOA rs309850 3- and 4-repeat polymorphisms have low and high activity, respectively, in the metabolism of monoamines (Hu et al., 2013). The MAOA rs1137070 C > T allele reduces MAOA enzyme activity (Shiels et al., 2008).

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