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제	목	Gene-environment interaction in the determination of plasma homocysteine levels.				
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Objective: Total plasma homocysteine (tHcy) level is an independent risk marker for cardiovascular disease, osteoporotic fractures, and Alzheimer disease. The aim of this study was to determine the effects of polymorphisms in 5,10-methylenetetrahydrofolate reductase (MTHFR) on total homocysteine (tHcy) in plasma in Korean adults and to investigate the interactions between genetic polymorphisms and environmental factors in determining tHcy levels.

Methods: This study included 1,543 subjects (707 men and 836 women; aged 20-74 years), who participated in the Thyroid Disease Prevalence Study, which compared the prevalence rate of thyroid disease in different regions and investigated the risk factors for chronic disease, such as cardiovascular disease, osteoporosis and dementia. This study was carried out in the Yeonggwang and Muan counties of Jeollanam-do Province, Korea, in July and August 2004. Homocysteine measurement was performed using a Fluorescent Polarization Immuno Assay (FPIA, Abbott Laboratories, Abbott Park, IL). The genotyping for MTHFR C677T polymorphism was performed by polymerase chain reaction(PCR) and restriction enzyme analysis. Genotyping for MTHFR A1298C was performed allelic discrimination to using dual-labeled probes containing locked nucleic acids in a real-time PCR assay.

Results: The median tHcy (and 5-95 percentiles) was 8.9 µmol/L (5.2 - 15.3 µmol/L) in men, and was 5.8 µmol/L (3.7-9.6 µmol/L) in women. The MTHFR C677T genotype frequencies for CC, CT, and TT were 33.8%, 48.3%, and 18.0%, respectively. The MTHFR A1298C genotype frequencies for AA, AC, and CC were 67.1%, 29.4%, and 3.6%, respectively. Individuals with the MTHFR 677TT genotype have significantly higher tHcy than with the 677CT and 677CC genotypes in both sexes. Smoking was positively associated with tHcy concentration, while alcohol and green tea consumption were negatively associated with tHcy concentration in men. In women, coffee consumption was negatively associated with tHcy concentration. The effect of MTHFR genotype on tHcy levels was modified by smoking status, intake of alcohol, intake of coffee, and intake of grean tea in men.

Conclusion: These data suggest that MTHFR polymorphisms have a significant effect on tHcy levels in Korean adults and that these effects are modified by demographic and environmental variables such as sex, smoking, alcohol, coffee, and green tea consumption