

POLYMORPHISMS OF DEBRISOQUINE HYDROXYLATION AND MARIJUANA PREFERENCE AMONG SUBSTANCE ABUSING ADOLESCENTS

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Polymorphisms of oxidative metabolism may have a role in drug abuse. We examined the relationship between phenotypic variations in debrisoquine (DBQ) hydroxylation (P4502D6) and marijuana preference among a group of male (n=88) and female (n=43) adolescents (15-19 years) who met DSM-III-R criteria for a Psychoactive Substance Use Disorder, and had some exposure to marijuana. Subjects identified their preferred drugs, and their recollection of subjective effects was elicited. After a monitored 72-hour drug abstinence interval, 10 mg of DBQ was orally administered and urine collected over 8 hours. Urinary DBQ and 4-hydroxy-DBQ were determined by HPLC, and metabolic ratios (MRs) were computed. MRs were clustered into Extensive (EM), Intermediate (IM) and Poor Metabolizer (PM) phenotypic groups by the group centroid method. Among males, no association was found between DBQ phenotype and marijuana preference. However, among females PM and IM metabolizers exhibited a distinct lack of preference for marijuana with 100% of those who preferred marijuana being EMs (Chi-square=3.24, df=2, $p<.05$). Significant inverse correlations between MR and measures of positive subjective effects of marijuana were also found among females. The results suggest that pharmacogenetic factors may be a component of the liability for abuse of specific drugs within defined populations.

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