Population frequencies of the A1 allele at the dopamine D2 receptor locus.

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Source
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Abstract
The reported association of a polymorphic allele at the dopamine D2 receptor locus (DRD2) and alcoholism has recently been the focus of considerable interest and controversy. Evidence both for and against an association of the A1 allele of the Taq1 A system have been reported. One of the inconsistencies in these studies is the frequency of the A1 allele in the controls. We undertook this study to determine the frequencies of the DRD2 A1 allele in different populations. The frequency of the DRD2 A1 allele was studied in 381 unrelated people from 16 different populations. On a global scale the frequency of the A1 allele was found to be dramatically different among the populations studied, from as low as 0.09 to as high as 0.75. Because of these significant differences an association study with this polymorphism must carefully control for ethnic origin of subjects and the results must be evaluated with caution.

Genetic, personality, and environmental predictors of drug use in adolescents.

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Source
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Erratum in

Abstract
During adolescence there is a significant increase in risk-taking behavior, including experimenting with alcohol and drugs, which can lead to drug dependence. A new hypothesis regarding the genetic mechanisms that lead to drug use is tested using adolescent Caucasian children of alcoholics (57 males, 54 females; mean age = 14.5 years) data. Variables included in the study were dopaminergic genes (ANKK1 Taq1 A, DRD2 C957T, DRD4 7R, COMT Val/Met substitution, and SLC6A3 9R) and a GABAergic gene (GABRB3), all combinations of genes, a count of the number of hypodopaminergic genotypes, personality traits, neurocognitive factors, depressive symptoms, and environmental factors. Separate predictive models were found for males and females. Hypodopaminergic functioning predicted drug use in males; however, in females, a deleterious environment was
the salient predictor. This preliminary study suggests that it is possible to identify children at risk for problematic drug use prior to the onset of drug dependence.

- THIRD REFERENCE

GENETIC ADDICTION RISK SCORE (GARS) ANALYSIS: EXPLORATORY DEVELOPMENT OF POLYMORPHIC RISK ALLELES IN POLY-DRUG ADDICTED MALES

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Journal: The IIJOAB Journal ISSN 0976-3104

Volume: 1; Issue: 2; Start page: 1; Date: 2010;

Original page

Keywords: Genetic Addiction Risk Score (GARS) | polymorphic genes | Neurotransmitters | Dopamine | Reward Deficiency Syndrome (RDS)

ABSTRACT

There is a need to classify patients at genetic risk for drug seeking behavior prior to or upon entry to residential and or non-residential chemical dependency programs. We have determined based on a literature review, that there are seven risk alleles associated with six candidate genes that were studied in this patient population of recovering poly-drug abusers. To determine risk severity of these 26 patients we calculated the percentage of prevalence of the risk alleles and provided a severity score based on percentage of these alleles. Subjects carry the following risk alleles: DRD2=A1; SLC6A3 (DAT) =10R; DRD4=3R or 7R; SHTTIRP = L or LA; MAO= 3R; and COMT=G. As depicted in table 2 low severity (LS) = 1-36%; Moderate Severity =37-50%, and High severity = 51-100%. We studied two distinct ethnic populations group 1 consisted of 16 male Caucasian psycho stimulant addicts and group 2 consisted of 10 Chinese heroin addicted males. Based on this model the 16 subjects tested have at least one risk allele or 100%. Out of the 16 subjects we found 50% (8) HS; 31% (5) MS; and 19% LS (3 subjects). These scores are then converted to a fraction and then represented as a Genetic Addiction Risk Score (GARS) whereby we found the average GARS to be: 0.28 low severity, 0.44 moderate severity and 0.58 high severity respectively. Therefore, using this GARS we found that 81% of the patients were at moderate to high risk for addictive behavior. Of particular interest we found that 56% of the subjects carried the DRD2 A1 allele (9/16). Out of the 9 Chinese heroin addicts [one patient not genotyped] (group 2) we found 11% (1) HS; 56% (5) MS; and 33% LS (3 subjects). These scores are then converted to a fraction and then represented as GARS whereby we found the average GARS to be: 0.28 Low Severity; 0.43 moderate severity and 0.54 high severity respectively. Therefore, using GARS we found that 67% of the patients were at moderate to high risk for addictive behavior. Of particular interest we found that 56% of the combined 25 subjects (Caucasian and Chinese) had a moderate to high GARS. Confirmation of these exploratory results and development of mathematical predictive values of these risk alleles are necessary before any meaningful interpretation of these results are to be considered.