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**Journal of =sychoactive Drugs**
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►Reward Deficiency Syndrome (RDS): A =iogenic Model for the Diagnosis and Treatment of Impulsive, Addictive, and =ompulsive Behaviors.

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►The dopaminergic system, and in particular the dopamine D2 receptor, =as been profoundly implicated in reward mechanisms in the brain. Dysfunction of the D2 dopamine receptors leads to aberrant =ubstance seeking behavior which includes but is not limited to alcohol, =rug, tobacco, and food and other related behaviors (pathological =ambling, Tourette's and attention deficit hyperactivity disorder). In =his paper we propose that genetic variants of the D2 dopamine receptor =ene and other "reward genes" are important common genetic =eterminants of the emerging concept first coined by Blum – "REWARD DEFICIENCY =YNDROME". This article reviews the results of studies concerning =articular classes of biological phenotypes that may have relevance to not =nly alcohol dependence but to the above mentioned related addictive, = compulsive and impulsive disorders. Broadly defined these =lasses include brain neurotransmitter systems and neuroelectric =otentials. Evidence is presented from many global scientific studies, =oncerning genotypic variation in severe alcoholics, high- risk relatives, psycho-stimulant abusers, opiate addicts, carbohydrate bingers, dependant tobacco smokers, polysubstance seekers, pathological =amblers, violent offenders schizoid/avoidant personality types and ADHD, Tourettes and Autism among other related RDS behaviors. The =esults of these studies strongly suggest that etiology of RDS is mediated =n part through sub-optimal neurotransmitter functioning, in particular = hypodopaminergic activity. The paper also points out the fact =hat genetic antecedents for RDS behaviors are polygenic in nature =nd multiple gene variants contribute to the overall variance of the = syndrome. Research opportunities are offered with respect to =pecific candidate genes that have been cloned from these =eurotransmitter systems that could be most fully utilized in both association =nd possibly family – based linkage studies, only if 1000's of =robands are employed in the latter case. Additional evidence is submitted, suggesting that characteristics of particular neuroelectric =otentials (e.g. the amplitude and the latency of the P300 components of =he event-related potential) may provide the cleanest dimension of =otential markers that could be used to identify children at risk for RDS. =he paper also discusses the conflicting findings with regard to the = association studies of the minor Taq1 A1 allele of the dopamine =2 receptor (DRD2) gene with alcoholism. The authors conclude that =eta analyses strongly favor the positive association and failure of association is due to failure to assess alcoholics for severity =f their disorder and to screen controls for substance use and others RDS = behaviors. The article favorably reviews data involving the use =f multiple modalities for the treatment of RDS including =hamacaceutical, nutraceutcal, neurofeedback, electrophysiological, auricular =herapy and chiropractic. Further studies involving well

defined animal =odels of RDS, such as the Lewis rat, showing hypodopaminergic limbic =unction, provides the field with a model to dissect the multiple genetic mechanisms involved in this complex disorder, possibly by =mploying Quantative Trait Loci experiments. Finally, multiple domains of =nquiry should not be viewed as “unfocused” but rather as an =conomical means for utilizing highly characterized samples of potential RDS =robands meeting rigorous research criteria.

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