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ABSTRACT

REWARD DEFICIENCY SYNDROME (RDS): A BIOGENIC MODEL FOR THE DIAGNOSIS AND TREATMENT OF IMPULSIVE , ADDICTIVE , AND COMPULSIVE BEHAVIORS.

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The dopaminergic system, and in particular the dopamine D2 receptor, has been profoundly implicated in reward mechanisms in the brain. Dysfunction of the D2 dopamine receptors leads to aberrant substance seeking behavior which includes but is not limited to alcohol, drug, tobacco, and food) and other related behaviors (pathological gambling, Tourette's and attention deficit hyperactivity disorder). In this paper we propose that genetic variants of the D2 dopamine receptor gene and other "reward genes" are important common genetic determinants of the emerging concept first coined by Blum – "REWARD DEFICIENCY SYNDROME". This article reviews the results of studies concerning particular classes of biological phenotypes that may have relevance to not only alcohol dependence but to the above mentioned related addictive , compulsive and impulsive disorders. Broadly defined these classes include brain neurotransmitter systems and neuroelectric potentials. Evidence is presented from many global scientific studies , concerning genotypic variation in severe alcoholics , high –risk relatives, psycho-stimulant abusers, opiate addicts, carbohydrate bingers, dependent tobacco smokers, polysubstance seekers, pathological gamblers, violent offenders, schizoid/avoidant personality types and ADHD, Tourettes and Autism among other related RDS behaviors. The results of these studies strongly suggest that etiology of RDS is mediated in part through sub-optimal neurotransmitter functioning , in particular a hypo-dopaminergic activity. The paper also points out the fact that the genetic antecedents for RDS behaviors are ***polygenic*** in nature and multiple gene variants contribute to the overall variance of the syndrome. Research opportunities are offered with respect to specific candidate genes that have been cloned from these neurotransmitter systems that could be most fully utilized in both association and possibly family -based linkage studies , only if 1000's of probands are employed in the latter case. Additional evidence is submitted , suggesting that characteristics of particular neuroelectric potentials (*e.g.* the amplitde and the latency of the P300 components of the event-related potential) may provide the cleanest dimension of potential markers that could be used to identify children at risk for RDS. The paper also discusses the conflicting findings with regard to the association studies of the minor *Taq1 A1* allele of the dopamine D2 receptor (DRD2) gene with alcoholism. The authors conclude that meta analyses strongly favor the positive association and failure of association is due to failure to assess alcoholics for severity of their disorder and to screen controls for substance use and other RDS behaviors. The article favorably reviews data involving the use of multiple modalities for the treatment of RDS including phamacaceutical , nutraceutcal, neuro-feedback, electrophysiological , auricular therapy and chiropractic . Further studies involving well defined animal models of RDS, such as the Lewis rat, showing hypodopaminergic limbic function, provides the field with a model to dissect the multiple genetic mechanisms involved in this complex disorder, possibly by employing Quantitative Trait Loci experiments . Finally, multiple domains of inquiry should not be viewed as " unfocused" but rather as an economical means for utilizing highly characterized samples of potential RDS probands meeting rigorous research criteria.