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GENETIC ADDICTION RISK SCORE ANALYSIS: HYPODOPAMINERGIC POLYMORPHIC RISK ALLELES IN POLYDRUG ADDICTED MALES AND MESO-LIMBIC DOPAMINERGIC AGONISTIC ACTIVATION BY NEUROADAPTAGEN AMINO-ACID THERAPY K. Blum^{1,2,3,4}, E. Stice⁵, Y. Liu¹, J. Giordano², S. Morse², J.A. Bailey¹, J. Thompson⁶, A. Smolen⁷, M. Oscar-Berman⁸, A. Bowirrat⁹, C. Allen¹⁰, M. Manka¹¹, B.W. Downs³, F. Fonari⁴, J. Tan¹², U.J. Damle¹³, E.R. Braverman^{13,14}

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Methods: The prevalence of seven risk alleles (DRD2=A1; SLC6A3 (DAT) =10R; DRD4=3R or 7R; 5HTTLPR = L or LA; MAO= 3R; COMT=G) and corresponding severity risk score (Low (LS) = 1-36%, moderate (MS) =37-50%, and high (HS) = 51-100%) were calculated. Group 1 consisted of 16 Caucasian male psycho-stimulant addicts, and Group 2 consisted of 10 Chinese male heroin addicts (9 were genotyped). qEEG and fMRI visualized the impact of Neuroadaptagen Amino-Acid Therapy complex on mesolimbic system activation. Results:

| Group | HS | HS Average GARS | MS | MS Average GARS | LS | LS Average GARS | Moderate to High Risk for Addictive Behavior | DRD2 A1 Allele |
|----------|-----|-----------------------|-----|-----------------------|-----|-----------------------|--|----------------------|
| 1 (n=16) | 50% | 0.58 | 31% | 0.44 | 19% | 0.28 | 81% | 56% |
| 2 (n=9) | 11% | 0.54 | 56% | 0.43 | 33% | 0.28 | 67% | 56% |

[Findings by Group]

74% of the combined groups had a moderate to high genetic addiction risk score (GARS). One acute dose of KB220-IV variant in heroin addicts having brain abnormalities was found to normalize qEEG. Additionally, a randomized double-blind placebo controlled study involving oral KB220-Z variant established qEEG normalization of reward circuitry in abstinent psycho-stimulant abusers (P < 0.03).

Conclusions: We cautiously suggest that long-term activation of dopaminergic receptors will lead to D2 receptor proliferation and enhanced "dopamine sensitivity," thus reducing aberrant craving behavior especially in carriers of the DRD2 A1 allele. Although supported by 20 clinical trials, KB220-Z awaits PET scanning to determine its chronic effects on D2 receptor numbers.