

Analysis of Mood Response to Tryptophan Depletion and Monoamine-Related Risk Genotypes

Holly A Garriock¹, Robert P Erickson¹, Joel Gelernter², Justin Tolman³, Adam Opbroek³, Pedro Delgado⁴, Francisco A Moreno³

¹University of Arizona Interdisciplinary Program in Genetics

²Yale University School of Medicine Department of Psychiatry

³University of Arizona Department of Psychiatry

⁴University of Texas Health Sciences Center at San Antonio

Introduction: Low levels of the neurotransmitter serotonin are associated with major depression. Many research groups have sought the cause of the serotonin-deficit by looking for associations of polymorphisms in single genes involved in the serotonin-signaling pathway using case-control studies. We analyzed our genetic data based on the number of risk alleles one might have that each contribute to the serotonin-deficit.

Methods: Thirty-eight Caucasian individuals in remission from unipolar depression were tryptophan depleted and genotyped for thirteen candidate genes: four directly related to serotonin function, six related to dopamine function, and three that play a role in many neurotransmitter systems. The change in depressive symptoms throughout depletion testing was assessed by the Hamilton Depression Rating Scale.

Results: Single-gene effects included AP2- β : $F = 2.993$, $df = 3$, 32 $p = .045$ and BDNF: $F = 15.743$, $df = 3$, 33 , $p < .001$. Individuals with a greater number of serotonin-risk genotypes experienced significantly more depression during depletion. The number of serotonin risk genotypes accounts for 21.6% of the variance in the change in depressive symptoms during depletion ($F = 9.906$, $df = 1$, 36 , $p = .003$). No association between dopamine-risk genotypes and depressive symptoms during depletion was detected.

Conclusions: The use of the depressive response during tryptophan depletion provides an objective, measurable phenotype and allows us to detect specific polygenic systems that contribute to the etiology of depression.

