

The WAGER, Vol 4(46) - The Genetic Plot Thickens

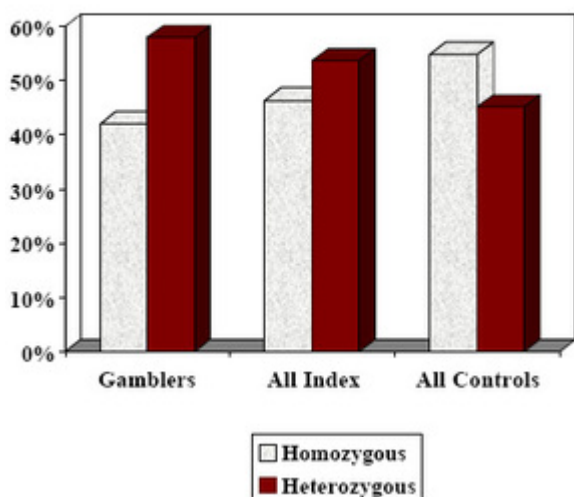
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[Editor's note: the United States Department of Energy publishes an excellent glossary of genetic terminology and a primer on molecular genetics. Both will be helpful to readers with no background in genetics]

Last summer, WAGER 3(30) presented David Comings's research relating variations of the DRD4 dopamine receptor gene with pathological gambling. In a more recent study, Comings and his colleagues advance their previous findings by greatly increasing their sample size and the breadth of their investigation. As in their past work, they look at the prevalence of seven different alleles of the DRD4 receptor gene in 737 control subjects and 707 index subjects (165 pathological gambling, 223 Tourette's, 52 ADHD, and 267 substance dependency). But this time, the authors looked at other genetic factors as well. Most salient is their examination of the zygosity of the genotypes of the DRD4 gene. A genotype is homozygous if the allele donated by the father is the same as the allele donated by the mother. A genotype is heterozygous if the allele donated by the father is different than the allele donated by the mother. [For an animated illustration of these principles, see the online version of this document]

Comings and his colleagues found that Homozygous Genotypes of the DRD4 Dopamine pathological gamblers have a significantly higher frequency of heterozygous genotypes than the control group. This phenomenon, called "positive molecular heterosis" by the authors, is illustrated in Figure 1. A similar effect was found for the index subjects as a whole, although an opposite effect was found for subjects with substance dependency. What does this mean? When considered in conjunction with other findings presented in the present article (which, for reason of space, are not discussed in this WAGER), the molecular genetics of pathological gambling may be considerably more complex than previously thought. While it is tempting to rejoice whenever new correlations are found between a particular genotype and a disorder, we must be cautious. The relationship, if there really is one, may be Gamblers All Index All Controls confounded, complicated, or otherwise modified by factors yet to be discovered.

Figure 1: Prevalence of Heterozygous and Homozygous Genotypes of the DRD4 Dopamine Receptor Gene (48bp)



Sources: Comings, D.E., Gonzalez, N., Wu, S., Gade, R., Muhleman, D., Saucier, G., Johnson, P., Verde, R., Rosenthal, R.J., Lesieur, H.R., Rugle, L.J., Miller, W.B. & MacMurray, J.P. (1999). Studies of the 48bp repeat polymorphism of the DRD4 gene in impulsive, compulsive, addictive behaviors: Tourette syndrome, ADHD, pathological gambling, and substance abuse. *American Journal of Medical Genetics*, 88: 328-368.

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