COMT Gene Variation in Attention Based Collegiate Sports

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Abstract

The COMT gene encodes an enzyme that mediates the degradation of dopamine, which is present in the pre-frontal cortex during periods of adverse stimuli. A single nucleotide polymorphism (rs4680) alters the rate of dopamine degradation between the two alleles of COMT. The slow acting enzyme includes a methionine at codon 158 (Met^{158}) and the fast acting enzyme includes a valine at codon 158 (Val^{158}). The fast acting allele gives an advantage in high stress circumstances, while the slow acting allele gives an advantage in memory and attention. Although COMT is well-studied gene, it is not known if either COMT allele confers an advantage in sports performance. In order to determine if the slow acting COMT allele gives an advantage in high-attention sports, we genotyped the COMT gene in athletes and compared the allele frequency to a control population. We hypothesized that student-athletes in high attention sports (softball, baseball, volleyball, and tennis) would have a higher frequency of the slow acting COMT allele as compared to controls. Seventy-one Division III student-athletes at the University of Wisconsin – Stevens Point from the softball, baseball, volleyball and tennis teams were compared to 350 control students from the University of Wisconsin-Stevens Point. Our results suggest that the slow acting COMT allele gives a slight advantage in baseball, while the fast acting allele is found with higher frequency in volleyball.

Background

Several factors influence athletic ability. In addition to environmental factors, genes play a significant role in predisposing an athlete for success in a given sport. The gene COMT (catechol-O-methyltransferase) determines the rate at which extracellular neurotransmitters are degraded in the prefrontal cortex, including the neurotransmitter dopamine. COMT is encoded by one of two alleles, the difference being a single nucleotide polymorphism (SNP) at codon 158. The rapid or slow degradation of dopamine is determined by which allele(s) an individual carries. The amino acid valine at codon 158 (Val^{158}) encodes a fast acting enzyme, while a methionine at the same codon (Met^{158}) encodes a slow acting enzyme.

The Val^{158} allele gives an advantage in high stress circumstances. This allele leads to the rapid breakdown of dopamine, and less neuronal activity in the prefrontal cortex which controls the stress response. Individuals who carry Val^{158} have higher pain tolerance and perform better under increased stimuli. This allele would be advantageous in high pressure situations and is often called the 'warrior' allele. Met^{158} is associated with lower pain tolerance, and decreased performance under pressure, but gives an advantage in memory and attention (Stein et al). Since dopamine is present longer with this allele, there is more neuron activity in the prefrontal cortex leading to better attention and memory. This allele would be advantageous in high attention tasks and cognition and is often called the 'worrier' allele. The differences between the Met^{158} and Val^{158} are highlighted in Table 1.

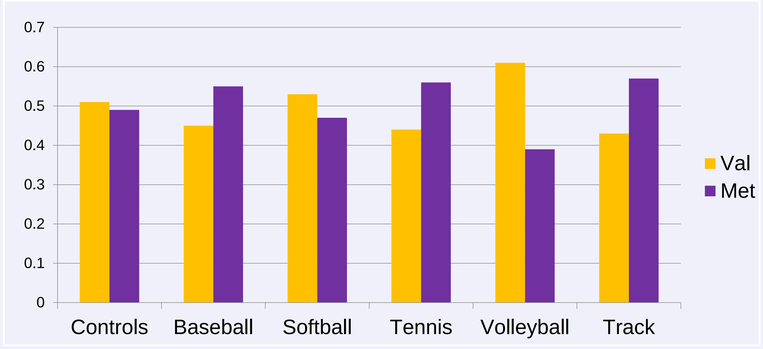
We hypothesized that student-athletes in high attention sports would have a higher frequency of the Met^{158} ('worrier') allele as compared to controls. To test this hypothesis we genotyped the COMT gene in 129 athletes from the softball, baseball, volleyball, tennis, and track teams at the University of Wisconsin-Stevens Point. We then compared these results to 304 control subjects taken from students at the University of Wisconsin-Stevens Point.

	Control					Athlete		
	Age	Caucasian	Sex	Sport Played	Varsity Athletes	Age	Caucasian	Sex
Total	20.4	92.40%	304	73%	46%	19.6	94.37%	71
Male	20.5	92.40%	117	80%	56%	20.21	100%	33
Female	20.4	92.40%	187	68%	40%	19.21	89.47%	38

Table 2. Demographics. Data is shown for male, female and combined. Caucasian represent the highest number of participants and ethnicity is shown as a percent of participants that were Caucasian. Control subjects are broken down as a percentage of those who play the sport for their high school as well as those who played a varsity sport for their high school.

Sport	n	Val158	Met158	P Value
Control	304	0.514	0.485	
Baseball	33	0.454	0.545	0.103
Softball	15	0.533	0.466	0.426
Tennis	9	0.444	0.555	0.460
Volleyball	14	0.607	0.392	0.588

Table 3. Sample Size, Allele Frequencies, and P Value. N represents the number of individuals in each group. Allele frequencies represent the total number of Val158 or Met158 within each group. P values were derived from a T-test comparing the frequency of the Val158 of each group to the control.



Graph 1. Allele Frequencies. The darker purple represents the allele frequency of the Val158 or 'warrior' allele and the lighter purple represents the frequency of the Met158 or 'worrier' allele.

Discussion

We hypothesized that student-athletes in high attention sports (softball, baseball, volleyball, tennis, and track) would have a higher frequency of the slow acting Met^{158} COMT allele as compared to controls, which may indicate that this allele confers an advantage to participants of that sport. To test this hypothesis we genotyped the COMT gene to determine if Met^{158} allele gives an advantage in these sports, as evident by an increased frequency of the studied allele.

Our results show no significant correlation of the Met^{158} allele among athletes within the high-attention sports analyzed in our study. Softball shows a slight shift, while volleyball shifts strongly, towards Val^{158} 'warrior' allele, but neither was significantly different from the control population. Neither team had a large sample size (15 from softball and 14 from volleyball), and larger sample sizes may reveal an advantage for the 'warrior' allele. Tennis, baseball, and track all show a shift toward the Met^{158} 'worrier' allele, but none were large enough deviations from the control group to suggest that the shift is caused by anything other than chance alone. These shifts are evident in Table 3 and Graph 1.

In conclusion, we were unable to accept our hypothesis because there was not enough significant difference in the allele frequency between our control population and athletes. The sample size was the main limitation to our study. The sample size of each sport would need to be much larger to determine if the Met^{158} ('worrier') allele of COMT contributes to athletic success in any way. The identification of genes related to athletic ability is most likely to occur at the elite level of competition. Since our study was restricted to Division III athletes we cannot rule out that COMT has no effect on athletic performance. Our data does reveal a trend towards different COMT allele that is promising, and more research could increase the number of study participants, or examine the COMT gene in elite athletes.

Val^{158}	Met^{158}
Warrior	Worrier
G	A
Fast Dopamine Breakdown	Slow Dopamine Breakdown
High Performance under adverse stimuli	Low performance under adverse stimuli
Disadvantage in memory and attention	Advantage in memory and attention

Table 1. COMT Description. A summary of the genotypic and phenotypic information of the COMT gene

Materials and Methods

Sample Collection

Surveys were given to all study participants regarding their age, ethnicity, academic major, and athletic participation. These demographics are shown in Table 2. 129 individual samples were collected from the athletes in baseball, softball (women's), tennis (women's), volleyball, and track (men's and women's). A total of 304 control samples were collected from students . All collection of human samples was approved by the University of Wisconsin-Stevens Point Institutional Review Board for the Protection of Human Subjects (submission #14-15.055).

DNA Isolation

Buccal cells were extracted with 10ml of 0.9% saline solution. Cells were centrifuged and pelleted cells were resuspended in 200µl TE buffer (Sigma-Aldrich, St. Louis, MO). DNA from athletes was extracted using the GeneJET Genomic Purification Kit (Thermal Scientific, Waltham, MA). DNA of control samples was extracted by adding 100µl of resuspended cells to 250µl 5% chelex solution (Sigma-Aldrich) and incubated at 100˚C for ten minutes. Cell lysate was centrifuged for three minutes at 14,000 rpm and kept at 4˚C until use.

Genotyping

Genotyping of the COMT allele was performed with allele-specific PCR. Primers used were described by Ruiz-Sanz et al. (2). Each reaction contained four primers: a control that produced a 686 bp product; a Val^{158} allele specific primer that produced a 509 bp product; and a Met^{158} allele specific primer that produced a 222 bp product. PCR reactions were carried out using GoTaq Mastermix (Promega, Madison, WI) with 0.5 µM primer, 5% DMSO, and 20-200 ng DNA. Following PCR, 20 µL PCR product was loaded into a 1% agarose gel and imaged with the Gel Doc EZ Imager (Biorad, Hercules, CA).

Statistical Analysis

For statistical analysis the COMT genotype was coded by the number of Val^{158} alleles (Val^{158} homozygous: 2; heterozygous: 1; Met^{158} homozygous: 0). A t-test compared each athlete group to the genotype of the control population. A p-value of less than 0.05 was considered significant.

References

1. Stein DJ, Newman TK, Savitz J, Ramesar R. Warriors Versus Worriers: The Role of COMT Gene Variants. Pearls in Clinical Science, 11:745-748)

2. Ruiz-Sanz JI, Aurrekoetxea I, Ruiz del Agua A, Begorña Ruiz-Larrea M. Detection of catecol-O-methyltrasferase Val158Met polymorphism by a simple one-step tetra-primer amplification refractory mutation system-PCR. Molecular and Cellular Probes, 21;202-207.

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