Single Nucleotide Polymorphism Within *VGLUT1* and Its Association Between Concussion Duration and Severity

Madura, S A*, McDevitt, J K*, Tierney, R T*, Mansell, J L*, Hayes, D J*, Krynestskiy, E§: *Department of Kinesiology, Temple University, Philadelphia, PA, § School of Pharmacy, Temple University, Philadelphia, PA

Context: Sport-related concussion is a resultant of a mechanical insult which alters neuronal structure and chemical balance, modifying how the brain transmits neurological responses. Genetic variations [i.e., single nucleotide polymorphism (SNP)] within the promoter region disrupt the amount of protein produced, which could affect an individual's susceptibility to neuronal injury and alter the healing response post head impact. **Objective:** To determine the association of a promoter SNP within *VGLUT1* (i.e., rs74174284) to concussion duration and severity. **Design**: A between subjects design. **Setting:** Athletes were diagnosed at Temple University Sport Concussion and Athletic Neurotrauma Center (Philadelphia, PA), and genetic analysis took place at Jayne Haines Center for Pharmacogenomics Drug and Safety Center of Temple University School of Pharmacy (Philadelphia, PA). **Participants:** Forty participants (29 males and 11 females, mean age 19.96 $\pm$ 6.28 yrs.) who sustained a head impact via a concussion mechanism. **Interventions:** Athletes diagnosed with a concussion were genotyped for the *VGLUT1* SNP, and followed prospectively to full return to play. A Hardy-Weinberg Equilibrium to ensure observed genotype frequencies were consistent with the general population genotypes. A 2x2 chi-square assessed the allele frequency of the *VGLUT1* SNP and concussion duration. Fisher's exact tests examined genotype frequency and concussion duration. Six independent t-tests and 3 ANOVAs analyzed Vestibular-Ocular Reflex (VOR), BESS, and ImPACT scores and concussion duration. Univariate and multivariate regression analyzed genotype association with concussion duration and severity. **Main Outcome Measure(s):** Dependent variables were concussion duration and severity, which were reported through the concussion center evaluation forms. **Results:** An association was found between the dominant genetic model (CC versus GG + GC; $p = 0.0179$) and recovery, where prolonged recovery was 5.60 times greater for those carrying the dominant allele. An association was also found between age and recovery, where prolonged recovery was 4.70 times greater for adult (19.96 $\pm$ 6.28 yrs.) athletes. An association was identified for ImPACT test motor speed scores in the dominant (CC = 33.38 $\pm$ 10.15, GG + GC = 41.59 $\pm$ 7.39, $p = 0.01$) and codominant (CC = 33.82 $\pm$ 10.00, GG = 40.25 $\pm$ 5.18, CG = 42.46 $\pm$ 8.82, $p = 0.03$) genetic models, where those carrying the CC had worse scores at initial assessment. **Conclusions:** This study was the first to investigate an association between rs7417284 SNP within *VGLUT1* and concussion severity and duration. Due to the association found within the common genotype, regulation of glutamate may be at maximum capacity and during a concussive event, the overload of glutamate may overtake the amount of glutamate *VGLUT1* vesicles can package. Based upon these findings, rs74174284 maybe a predictive genetic marker for identifying athletes who a more susceptible for altered recovery times and more severe symptoms. **Key Words:** genetics, SLC17A7, rs74174284, prolonged recovery, head impact. **Word Count:** 455.