Malic enzyme 2 and genetic generalized epilepsy

William C. L. Stewart, Meng Wang and **David A Greenberg**
The Abigail Wexner Research Institute at Nationwide Children's Hospital, USA

Genetic generalized epilepsy (GGE) is a highly heritable condition (h^2=66%) consisting of epileptic syndromes with overlapping symptoms. Previous studies (both linkage and association) identified malic enzyme 2 (ME2) as a candidate susceptibility gene for adolescent-onset GGE. To definitively test *ME2's* influence on GGE, we used three different approaches. First, we compared a newly recruited GGE cohort with an ethnically matched reference sample from 1000 genomes, using an efficient test of association (POPFAM+). Second, in a previously collected data set, we replaced the original controls with ethnically matched reference samples to minimize the confounding effect of population stratification and we used POPFAM+ in the re-analysis. Third, in a post hoc analysis of healthy human pre-frontal cortex, we identified single nucleotide polymorphisms (SNPs) influencing ME2 messenger RNA (mRNA) expression and then, we tested those same SNPs for association with GGE in a large case control cohort. In the analysis of our newly-recruited GGE Cohort, we found a strong association between an ME2 SNP and GGE (p =0.0006 at rs608781). In the re-analysis of previously collected data, we confirmed the Greenberg *et al.,* (2005) finding of a GGE associated *ME2* risk haplotype. Finally, in the post hoc ME2 expression analysis, we found evidence for a possible link between GGE and *ME2* gene expression in human brain. Overall, our research (and the research of others) provides compelling evidence that ME2 influences adolescent onset GGE susceptibility.

Biography

William C. L. Stewart has completed his PhD in Statistics from the University Washington in 2005, and finished his Postdoctoral studies in the Biostatistics Department at the University of Michigan in 2008. He is a Principal Investigator at the Abigail Wexner Research Institute of Nationwide Children's Hospital. He is an Assistant Professor of Statistics and Pediatrics at Ohio State University. He has published more than 30 papers in peer-review journals and has served on the Editorial Board of Frontiers in Genetics for nine years.

William.Stewart@nationwidechildrens.org

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