TITLE:

Effects of genetic variation in LIMK1 on white matter microstructure: evidence from partial deletions of the William’s syndrome chromosome region and healthy controls

ABSTRACT

Williams syndrome (WS) is caused by a large hemideletion (1.5-1.8 Megabases) including approximately 28 genes on chromosome 7q11.23. It is associated with intellectual disability, alterations in social cognition (excessive friendliness), psychiatric phenotypes (e.g. phobias for non-social stimuli) and a characteristic impairment in visuo-spatial construction. Previous research demonstrated complex alterations in the white matter organization of participants with WS, either with normal or reduced intelligence quotient (IQ) and generated the hypothesis that one or more of the hemideleted genes could be responsible for alterations in axonal guidance underlying the alterations of white matter. In this study, we combine diffusion imaging data from twelve individuals with partial deletions of the Williams syndrome chromosome region (WSPD group), all of whom had a deletion of LIMK1, and association between a single nucleotide polymorphism (SNP rs710968) in the LIMK1 promoter and white matter organization in healthy volunteers. We found a diffuse reduction of white matter anisotropy in the WSPD group compared to controls (p=0.0003), which was correlated with visual construction performance (p=0.012). In 81 healthy volunteers, we found that the CC genotype of rs710968 was associated with reductions in white matter anisotropy as compared to T allele carriers (p=0.0037). In a concomitant study, this SNP was associated with reduced gray matter volume in the parietal lobe and altered expression of a novel LIMK1 isoform. This evidence supports a role of LIMK1 in altering white matter microstructure and visuospatial construction in WS.

Brief CV

Dr. Marenco completed his MD at the University of Genova, Italy and went on to obtain specialty training in Clinical Neurophysiology (University of Genova) and Psychiatry (University of Maryland in Baltimore, USA). He has completed fellowships in clinical research in nuclear medicine at Johns Hopkins University and in schizophrenia imaging at the National Institute of Mental Health. Since 2004 he has worked as a staff clinician at the NIMH, Clinical Brain Disorders Branch. Dr. Marenco has more than 60 publications to his name and his research has been primarily dedicated to magnetic
resonance imaging with diffusion tensor imaging and spectroscopy. He has applied these techniques primarily to genetic association studies and the study of schizophrenia biology.

**Recent Publications**


