Diffusion Imaging in Individuals with Partial Deletions of the Williams Syndrome Critical Region

Poster No:

331

On Display:

Wednesday, June 29 & Thursday, June 30

Stand-By Time:

Thursday, June 30: 10:30 – 13:30

Authors:

Dharshan Chandramohan[1], Matthew Geramita[1], Lindsay Walker[2], Katherine Roe[3], Shane Kippenhan[3], Aarthi Padmanabhan[3], Phillip Kohn[3], Carolyn Mervis[4], Ariel Pani[5], Colleen Morris[6], Daniel Weinberger[7], Carlo Pierpaoli[2], Stefano Marenco[1], Karen Berman[3]

Institutions:

[1]Unit on Multimodal Imaging Genetics, CBDB, NIMH-IRP, Bethesda, MD, [2]Section on Tissue Biophysics and Biomimetics, NICHD-IRP, Bethesda, MD, [3]Section on Integrative Neuroimaging, CBDB, NIMH-IRP, Bethesda, MD, [4]Neurodevelopmental Sciences Lab, University of Louisville, Louisville, KY, [5]Dept. of Biochemistry and Molecular Biology, University of Louisville, Louisville, KY, [6]Genetics Division, Dept of Pediatrics, University of Nevada School of Medicine, Las Vegas, NV, [7]GCAP/CBDB, NIMH-IRP, Bethesda, MD

Introduction:

Williams syndrome (WS) is a rare neurodevelopmental disorder resulting from hemizygous microdeletion of ~25 genes on chromosome 7q11.23. Individuals with WS usually exhibit mild to moderate intellectual disability and pronounced difficulty on tests of visuospatial construction. Prior Diffusion Tensor Imaging (DTI) studies have established that WS is associated with altered white matter (WM) integrity. Studying individuals with partial deletions (PD) in the WS critical region (WSCR) could provide insight into the role of a smaller set of genes within that region.

Methods:

Eleven individuals (9 females; mean age=36 ±13(SD) years) with PDs in the WSCR participated in this study. Participants had IQs within the normal range (mean=96.7 ±11.3), cognitive profiles consistent with the WS pattern, and varying 7q11.23 deletions which included the elastin (ELN) and LIM-domain kinase 1 (LIMK1) genes; none of the deletions included GTF2IRD1 or GTF2I. Five participants had deletions of only ELN and LIMK1. Eleven healthy individuals matched for age (mean=36 ±11 years), IQ (mean=99.6 ±8.9), and gender (7 females) served as the control group.

Diffusion Weighted Images (DWI) were acquired on a GE Signa 1.5T Scanner (2x2x2 mm resolution, 120 gradient directions, b-values between 0 and 1200). DWIs were corrected for head movement and eddy currents using TORTOISE [Pierpaoli et al. 2010].

Fractional anisotropy (FA) maps were derived using TORTOISE and were registered in a common space with Tract Based Spatial Statistics (TBSS [Smith et al. 2006], part of FSL [http://www.fmrib.ox.ac.uk/fsl/]). Nonparametric statistical tests were performed using FSL's randomise procedure with 2000 permutations, using threshold free cluster enhancement for family-wise error corrections of multiple comparisons over the whole brain.

Results:

We observed significant reductions of FA throughout the brain in PD individuals relative to controls (Fig. 1). 71% of the voxels in 48 major tracts were significant at a threshold of $p<0.01$, with peaks of significance in the right cingulum bundle, right external capsule and left internal capsule, which contained the most significant voxel (MNI coordinates: x=-40,y=-38,z=-3).

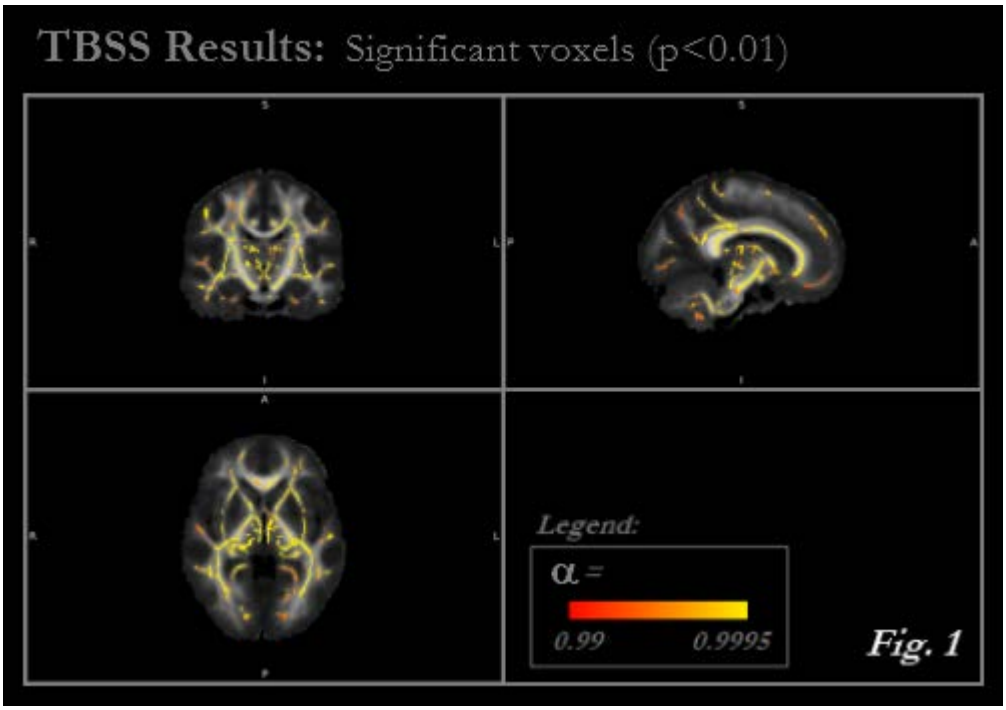
Conclusions:

Our results suggest that alterations in WM integrity in WS are related to a subset of genes in the WSCR. Since LIMK1 and ELN are the only deleted genes common to our entire PD group these findings implicate these two genes in particular. More work is necessary to understand the impact of LIMK1 and nearby genes

on WM structure as measured by DTI.

Genetics:

Neurogenetic Syndromes



Abstract Information

References

Pierpaoli, C. (2010), 'TORTOISE: an integrated software package for processing of diffusion MRI data', ISMRM 18th annual meeting, Stockholm, Sweden, #1597

S.M. Smith, S.M. (2006), 'Tract-based spatial statistics: Voxelwise analysis of multi-subject diffusion data', NeuroImage, vol. 31, pp. 1487-1505.