White Matter and Cortical Abnormalities in Williams Syndrome Detected by Diffusion Tensor Imaging.

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\textbf{INTRODUCTION:} Williams Syndrome (WS) is a unique combination of striking behavioral abnormalities, such as hypersociability, and characteristic neurocognitive loss, such as severe visuospatial construction deficit, raising fundamental questions about the mechanisms of the brain modularity. Regardless of morphometric and functional studies accessing cortical differences in WS patients, there are only a small number of studies reporting the status of the white matter. Here, we combined DTI, DTI based brain atlas, and large-deformation diffeomorphic metric mapping (LDDMM) to access shape and diffusivity in various white matter structures in WS patients' brains. LDDMM achieves an accurate level of normalization that allows warping an anatomical atlas, thereby automatically segmenting the white and gray matter into many functional units. We applied this Atlas-based approach (ABA) and voxel-based analysis (VBA) to investigate the status of the cortex and white matter structures related to physiopathological and clinical findings characteristics of this disease.

\textbf{METHODS:} 8 patients with WS (3 male, ages ranging from 12 to 27 years old, mean 18.4) and 8 healthy controls paired by age and gender were included in this study. Images were acquired using a 1.5T scanner with b=700s/mm\textsuperscript{2}. Nonlinear transformations between each subject's data and a single subject atlas were obtained using fractional anisotropy (FA) and b\textsuperscript{0} based (dual contrast) LDDMM. The atlas contains detailed parcellation of 176 white and gray matter structures. By warping our atlas to each subject original space we measured size, FA, apparent coefficient diffusion (ADC), parallel diffusivity (\lambda_{II}, the primary eigenvalue) and perpendicular diffusivity (\lambda_{III}, the average of the secondary and tertiary eigenvalues). The same parameters were analyzed by VBA. We used the Jacobian determinants of the LDDMM matrix to access differences in size. Wilcoxon Rank Sum test was carried out to access differences between groups with p value less than 0.1 after correction for multiple comparisons by false discovery ratio.

\textbf{RESULTS:} Total brain, CSF, and cortex volume were significantly smaller in WS. In both VBA and ABA (Figure 1), cortical regions in parietal and occipital lobes, suprana orbital and middle frontal gyri, basal ganglia, diencephalon, left internal and external capsules, portions of corona radiate and genu of corpus callosum were smaller in WS. Two focal regions, in pre-cuneus and forceps major at left and in the projection of superior longitudinal fasciculus (SLF) at right, were bigger (Figure 1 and 2). ABA showed increased FA in the projection of SLF, inferior longitudinal fasciculus (ILF), posterior thalamic radiations, fronto-occipital fibers and supra-orbital gyrus at right, cortex of superior temporal gyrus at left and caudate nucleus, bilaterally. Right SLF and cingulum also had significantly increasing of \lambda_{II} (Figure 3).

\textbf{DISCUSSION:} Reduction in parietal, occipital and orbital cortex was described before in WS, associated with debilities in fronto-occipital circuit and with anomalous parietal lobe gyriﬁcation. The enlargement of right SLF and other regions associated to visuospatial function were not reported in the past. Increased FA of the right SLF was showed in a previous study and conﬁrmed here. The known reduced leftward asymmetry of the planum temporal in WS can be responsible for these findings as well as the FA increase in other parts of right fronto-occipital tract and superior temporal cortex at left. The reduction of basal ganglia and FA increase in caudate, this latter also unexpected, can be related to alterations in fronto-striatal connections described in WS. Changes in cingulum diffusivity are in accord with functional studies where abnormal activation occurred in areas involved with social behavior.

\textbf{CONCLUSION:} Based on DTI and highly nonlinear normalization methods, we observed abnormalities in cortical and white matter regions in the WS population. These findings are compatible with the physiopathological and clinical characteristics of this disease, which include impairment of functional systems responsible for abilities such as visuospatial notion, language and socio-comportamental behavior.

\textbf{BIBLIOGRAPHY:}


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