

# Diffusion Tensor Imaging of Rett Syndrome

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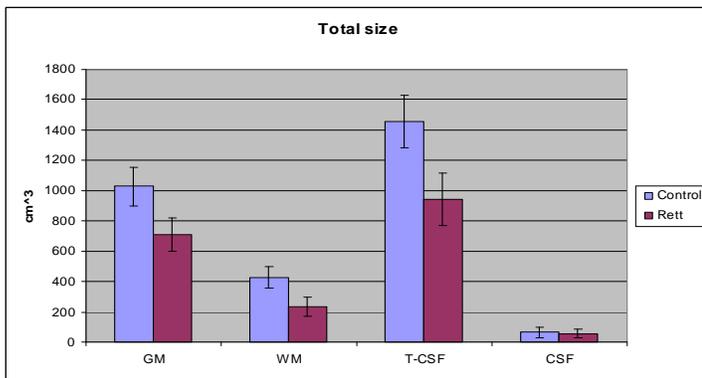
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## INTRODUCTION

Rett Syndrome (RTT) is a neurological disorder primarily affecting females, characterized by acquired microcephaly, loss of purposeful hand skills, and gait apraxia [1]. Previous imaging studies attempted to quantify global size alterations in RTT. In this study, we are using Diffusion Tensor Images (DTI) and an atlas-based quantification approach to investigate the status of various structures in the gray and white matter. Our primary interest is to investigate if the microcephaly is due to atrophy of specific brain regions. To test this hypothesis, the brains were normalized to the JHU atlas using the Large Deformation Diffeomorphic Metric Mapping (LDDMM), followed by automated brain segmentation. Various properties of each segment were then quantified.

## METHODS

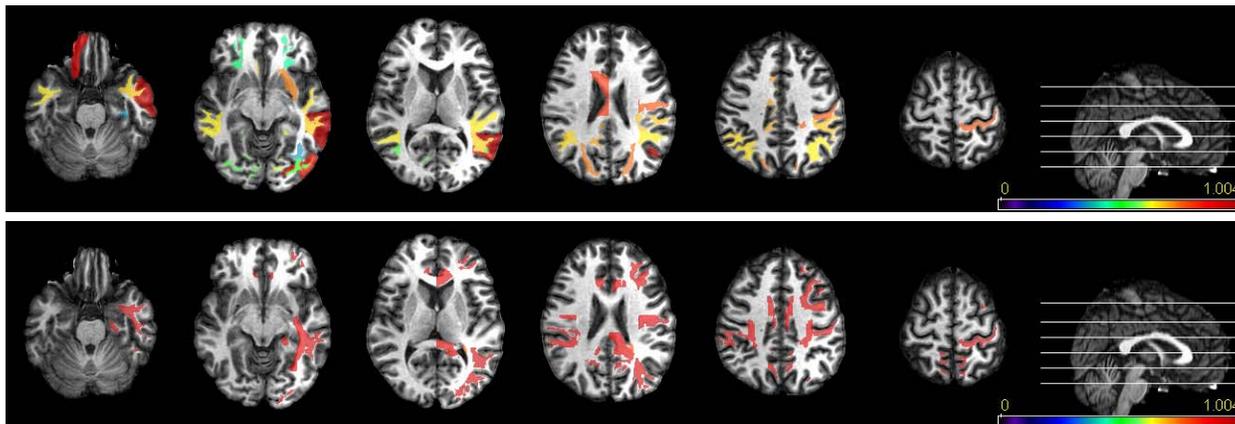
Images from RTT patients (n=9) (age ranging from 2 to 8 years old, mean 4) and gender and age matched controls (n=9) were acquired using 1.5T scanner with  $b=700\text{s/mm}^2$ . Nonlinear transformations between each subject's data and a single subject atlas were obtained using fractional anisotropy (FA),  $b_0$  and trace (the sum of eigenvalues) based on multi-contrast LDDMM. The atlas contains detailed parcellation of 176 white and gray matter structures. By warping our atlas to each subject's original space we measured size and FA. Atlas-based statistical analysis was carried out using non-parametric Wilcoxon rank sum test on each region to assess differences between groups with p-value less than 0.01.



**Figure 1:** Volumes of the entire GM, the WM, the total brain (not including the CSF), and the CSF.

## RESULTS

The measurements of the overall brain size (gray matter, white matter, and CSF) confirmed the overall decrease in brain size in the gray matter (GM), as well as the white matter (WM) [2-3]. (Fig.1). Results of regional size measurements detected 24 regions with significant difference, all of which were smaller in RTT subjects. Most of the regions (20) were in WM, particularly in distal white matter of the occipital, parietal, and temporal lobes (Figure 2). The regions included inferior fronto-occipital fasciculus, body of corpus callosum, WM of lingual, superior occipital, inferior occipital, supramarginal, angular, middle fronto-orbital, lateral fronto-orbital, middle temporal, superior temporal, fusiform, post-central, and cingulum gyrus, and GM of inferior occipital, middle temporal, and middle fronto-orbital gyrus. We found a 4% average reduction in FA values of the entire white matter and in 18 regions (14 left side, 4 right side) a 10% average significant ( $p<0.01$ ) reduction (Figure 3). Regions of significant reduction included WM of pre-cuneus, supramarginal, middle frontal, middle occipital, inferior temporal, middle temporal, post-central, and parahippocampal gyrus, superior longitudinal fasciculus, cingulum gyrus, sagittal striatum, tapatum, splenium and genu of corpus callosum.



**Figure 2:** Regions of significant size difference ( $p<0.01$ ). Colors represent ratio Rett/Control.

**Figure 3:** Regions with significant difference in FA ( $p<0.01$ ). Colors represent ratio Rett/Control.

## DISCUSSION AND CONCLUSION

Our findings show that the reduction in brain size is most notable in the occipital, temporal, and parietal regions. In many regions, the brain size decrease was accompanied by decrease in FA signal. The significant size and FA losses are mostly in the distal white matter regions close to the cortex. The FA decrease can be related to changes in axonal organization and myelination status. Our results suggest non-uniform white matter abnormalities in the RTT patients. The atlas-based segmentation of DTI data enabled us to study the status of intra-white matter structures. The drawback of this atlas-based approach is that if abnormal regions in RTT are confined to a small region, the averaging of all pixels within one structural unit may lead to lower sensitivity. Overall, however, the results from the study show that the method of atlas-based statistical analysis is a powerful screening method to assess size and fractional anisotropy differences in different pathologies.

## REFERENCES

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