Analysis of Diffusion Tensor Imaging for Subjects with Down Syndrome

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Introduction:

Down syndrome (DS) is the most common chromosome abnormality in humans. It is typically associated with delayed cognitive development and physical growth. DS is also associated with Alzheimer-like dementia [1]. In this study we analyze the white matter integrity of individuals with DS compared to control as is reflected in the diffusion parameters derived from Diffusion Tensor Imaging. DTI provides relevant information about the underlying tissue, which correlates with cognitive function [2]. We present a cross-sectional analysis of white matter tracts of subjects with DS compared to control.

Methods:

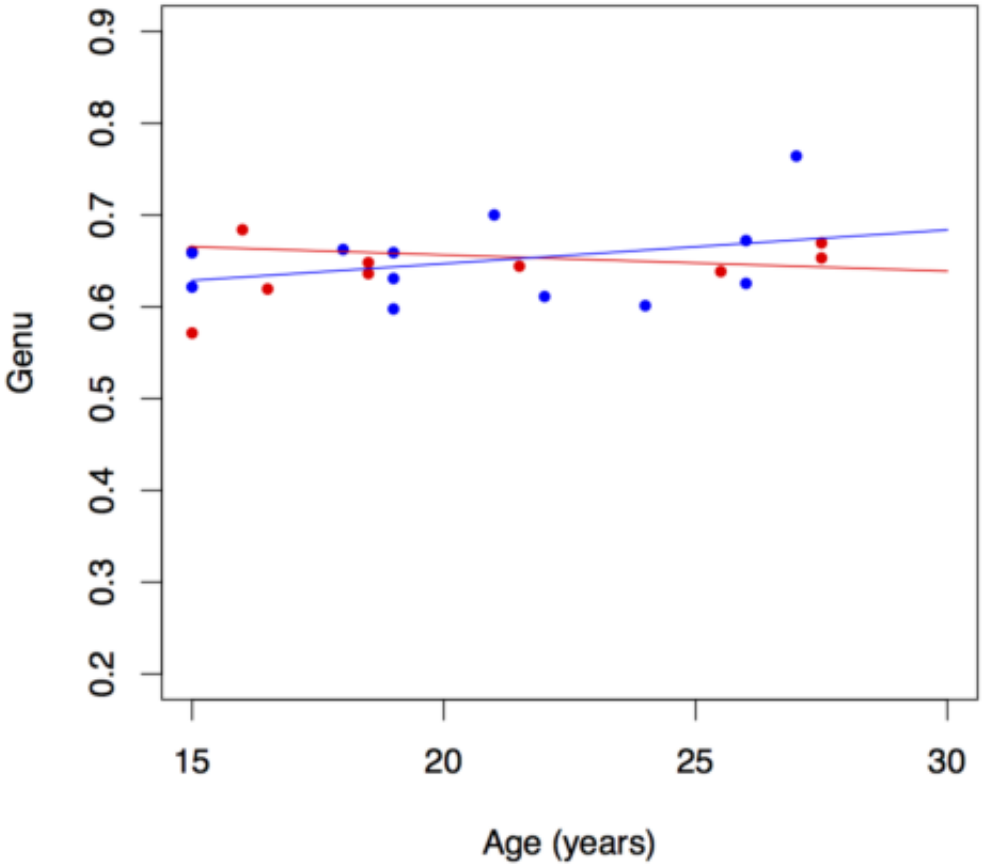
We study a population of 25 adults composed of 12 healthy controls (age 21 +/- 3.97) and 13 subjects diagnosed with Down syndrome (age 26.2 +/- 5.12). Each subject has diffusion tensor imaging (DTI) scans at different ages that capture different stages of development.

We construct an unbiased atlas of adult brains as a population template using the method described by Joshi et al. [3]. Diffusion tensor images of the subjects were mapped to the reference space defined by this template. White matter label maps developed and disseminated by Mori et al. [4] were also registered to this template [5][6]. The labeling of regions in the atlas space allows for automatic partitioning of each subject's scans. Fractional anisotropy (FA) were extracted from each region and compared between subjects with Down syndrome and control. False discovery rate was used to adjust for multiple comparisons.

Results:

We performed white matter analysis on the following brain regions: anterior limb of internal capsule (ALIC, right and left), posterior limb of internal capsule (PLIC, right and left), body of corpus callosum (BCC), genu, splenium, external capsule (ExCap, right and left), and posterior thalamic radiation (PTR), which includes the optic radiation.

Cross-sectional FA trajectories differ significantly in controls and DS subjects in the intercept term for ALIC R, Genu, ExCap L, PTR R and PTR L. Opposite patterns of development between controls and DS were observed in almost all the regions except for the left ALIC (ALIC L). FA tends to increase with age for the control group, whereas FA for subjects with Down syndrome tends to decrease with age with the exception of ALIC L which showed increasing trend for both populations. However, we didn't observe any significant differences in the slopes between these two groups which could be due to the small sample size and high variability between subjects. We observed only group-by-age differences for left ExCap (ExCap L). Estimated parameters for linear regression along with p-values are shown in Table 1 and 2.


Genu
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
15
20
25
30
Age (years)

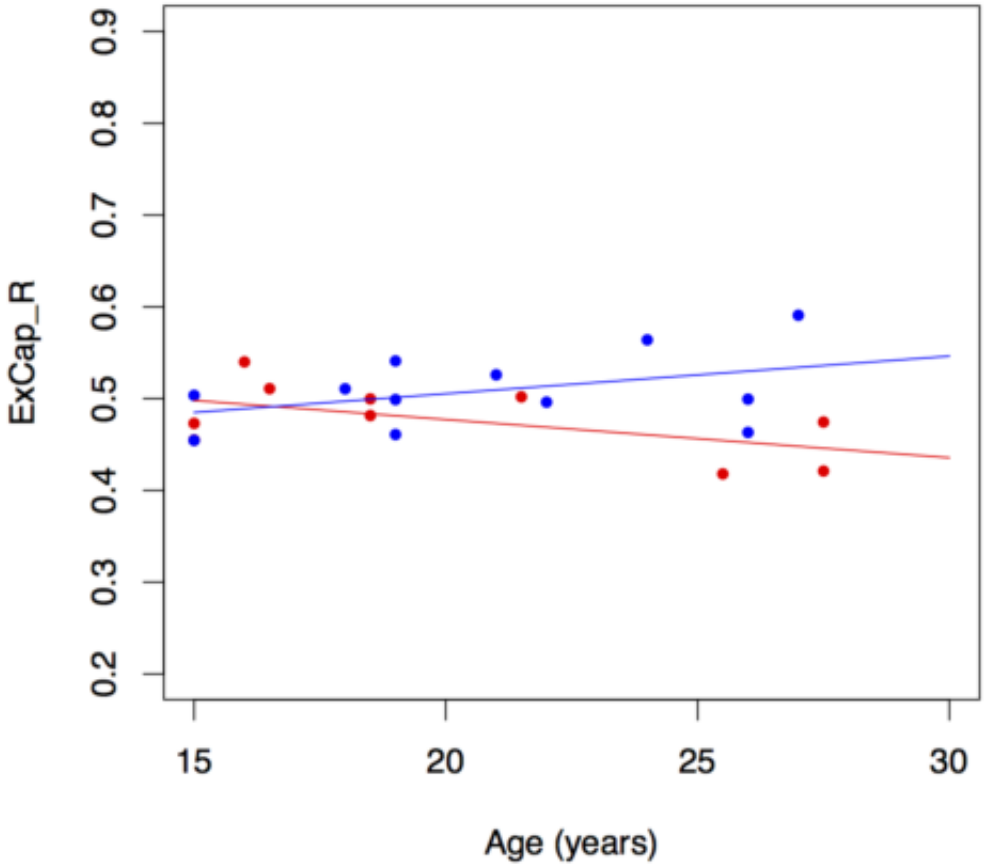


Table 1: Fitting parameters for each tract are shown for the equation FA = A+B*Age+C*Group+D*Age*Group

	A	B	C	D
ALIC R	0.51582	-0.00552	-0.07864	0.00628
ALIC L	0.30662	0.00407	0.07685	-0.00316
PLIC R	0.71960	-0.00707	-0.22322	0.01133
PLIC L	0.58940	-0.00115	-0.06369	0.00385
BCC	0.69203	-0.00177	-0.11845	0.00545
Genu	0.48337	-0.00567	-0.10535	0.00743
Splenium	0.58125	-0.00417	-0.11411	0.00574
ExCap R	0.56047	-0.00416	-0.13699	0.00826
ExCap L	0.66670	-0.01032	-0.20480	0.01325
PTR R	0.61590	-0.00697	-0.12850	0.00884
PTR L	0.56880	-0.00821	-0.13351	0.00989

Table 2: Anova Analysis between subjects with Down Syndrome and control
Significant differences p < 0.05 are highlight in red.

	Group difference in slope, raw p	Group difference in slope, adjusted p	Group difference in intercept, raw p	Group difference in intercept adjusted p	Group difference in group-by-age interaction, raw p	Group difference in group-by-age interaction, adjusted p
ALIC R	0.1480	0.2872	0.0010	0.0052	0.0337	0.0742
ALIC L	0.0476	0.2500	0.3715	0.5838	0.3429	0.3570
PLIC R	0.3366	0.4715	0.8632	0.9495	0.0657	0.1072
PLIC L	0.7410	0.9057	0.4629	0.6365	0.3570	0.3570
BCC	0.9845	0.9845	0.6608	0.8076	0.2417	0.2954
Genu	0.3429	0.4715	0.0191	0.0420	0.0682	0.1072
Splenium	0.0682	0.2500	0.9543	0.9543	0.2187	0.2954
ExCap R	0.8307	0.9138	0.0577	0.1057	0.0181	0.0511
ExCap L	0.0452	0.2500	0.0015	0.0056	0.0021	0.0228
PTR R	0.1566	0.2872	0.0046	0.0127	0.0186	0.0511
PTR L	0.0975	0.2681	0.0004	0.0046	0.0098	0.0511

Conclusions:

Our study shows a decrease in FA values of subjects with DS compared to control, which may be due to an earlier aging process in subjects with Down syndrome. DS subjects show cognitive differences that can be characterized in the white matter integrity of specific brain connectivity pathways. Diffusion tensors in white matter can serve as a surrogate biomarker of specific aspects of cognitive development in DS.

Imaging Methods:

Diffusion MRI

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