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Characterization of individual DTI measurement age trajectories in a longitudinal study of autism spectrum disorder

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MAIN TAKEAWAY

Individuals with autism spectrum disorder exhibit significantly different and more variable **longitudinal** trajectories of DTI measures compared to typically developing adolescent children and young adults.

ANALYSIS CODE

https://github.com/nadluru/ismrm2021

SYNOPSIS

- Investigated patterns of individual rates of change of diffusion tensor imaging (DTI) measures computed from a longitudinal study of autism spectrum disorder (ASD).
- The temporal mean and temporal rates of change of DTI were estimated for regions of white matter for individual subjects.
- The distributions of the individual longitudinal slopes versus mean measures for ASD and typically developing controls (TDC) were mapped and compared, revealing group differences in the distributions with generally greater heterogeneity in ASD group.

INTRODUCTION

- Autism spectrum disorder (ASD) is a heterogeneous disorder with highly variable outcomes.
- Previous work looked at these heterogeneous effects at the overall group level, and not necessarily at an individual level.
- Measurements of individual variation in ASD may help identify phenotypical subgroups and guide the development of personalized therapies or interventions.

Abbreviation	Region name
GCC	Genu of the corpus callosum
BCC	Body of the corpus callosum
SCC	Splenium of the corpus callosum
rALIC	Anterior limb of the internal capsule (right)
lALIC	Anterior limb of the internal capsule (left)
lSLF	Superior longitudinal fasciculus (left)

Please move cursor over figures for additional details when viewing in Adobe.
Poster checked for accessibility. **Poster session: Diffusion in the Brain.**

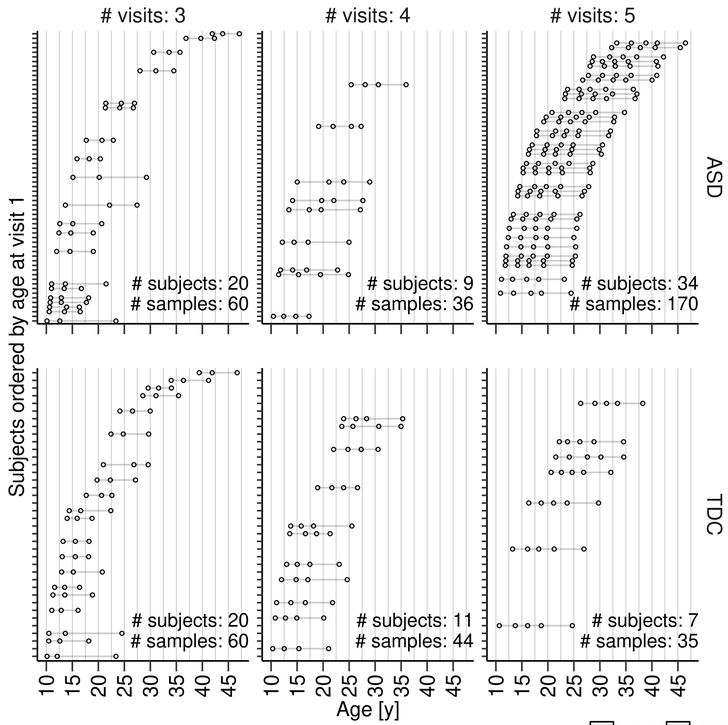

Figure 1. Overview of the samples from the accelerated longitudinal design (ALD) analyzed in this study. An ALD helps investigate subject level rates of change and temporal averages that even a large cross-sectional study cannot easily empower. Assuming a moderate acceleration in the cohort, an ALD makes such investigation over longer age ranges feasible, compared to synchronized longitudinal studies.

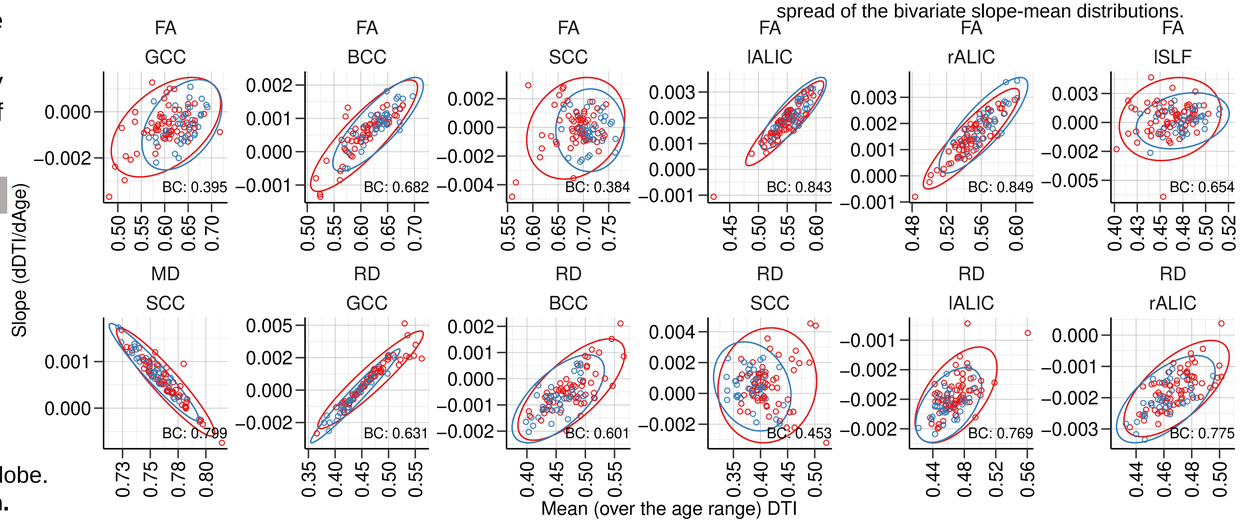

Figure 2. Gaussian contours (at 2σ) were overlaid on the distributions to visually assess the normality and spread of the bivariate slope-mean distributions.

METHODS

- **DIFFUSION WEIGHTED IMAGING (DWI)** data were acquired with b=1000 $s \cdot mm^{-2}$,12 directions, and 2×2×2.5 mm^3 resolution.
- **DESIGNER** based in-house pipeline for DTI processing.
- **LINEAR MIXED MODELS** to estimate the annual rates of change of median FA, MD and RD in regions of the JHU white matter atlas.
- **BHATTACHARYYA COEFFICIENT (BC)** to assess the amount of overlap of ASD and TDC.
- **HOTELLING T^2** statistical testing.
- **FALSE DISCOVERY RATE (FDR)** using the Benjamini Hochberg (BH) procedure.

RESULTS

- BC of the bivariate distributions show the amount of overlap between the distributions.
- Bivariate distributions show greater heterogeneity in the ASD group.
- Statistically significant differences, at FDR adjusted p≤0.05, were found for all the sub-fields of the corpus callosum (CC), i.e., genu, body and splenium regions and both FA and RD.
- The results are consistent with the known literature especially in showing that the corpus callosum is an important white matter pathway in contrasting ASD and TDC.
- The left but not right, superior longitudinal fasciculus was statistically significant indicating consistency with the language related findings in the autism literature.
- It is also interesting to note that FA and RD were the more sensitive than MD.
- While the rates of change alone might not be distinguishing between the ASD and TDC populations, when they are lifted to the bivariate space of temporal rate and temporal mean, we are able to elucidate the heterogeneity differences between the groups.

CONCLUSIONS

- Annual rates of change in DTI (slopes) derived from longitudinal data along with mean DTI over time provide useful markers when looked at jointly.
- It is interesting that there is more individual variability in the ASD group, not just group differences. Ultimately, this may help to identify phenotypes of ASD with faster or slower changes, etc.
- Currently, mixed models were used with only age and an overall intercept as fixed terms in the slope models and only an overall intercept as a fixed term for the mean models.
- Future research entails investigating the variability in estimation of the slopes and means and the best way to minimize systematic biases due to additional confounding fixed factors.

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