Age-Related Differences in Adolescent Brain Microstructure: Initial Findings from National Consortium on Alcohol & Neurodevelopment in Adolescence

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Investigate Aging of the White Matter Microstructure in Adolescents
Overview

• **NCANDA Data Acquisition**
• **DWI Specific Processing**
• **Current Findings (N=671)**
Monitoring brain development of 831 adolescence over a 5 year period across 5 sites
NCANDA Collection Sites

Sites collect:
- Demographic Information
- Clinical Data
- Neuropsychological Test Scores
- MRI
  - Structural
  - Diffusion
  - Functional
NCANDA – Informatics Platform

Robustly and coherently fusing data across time, sites, and modalities
White matter contains axons that group together to bundles connecting gray matter regions

Fibers restrict diffusion of water molecules
Diffusion Weighted Imaging

Measure the rate of diffusion within white matter by varying gradient direction of scanner’s magnetic field.

Ellipsoid represents diffusion direction at location.
Diffusion Weighted Imaging

Summarize diffusion via Fractional Anisotropy (FA)

\[ FA = \frac{1}{2} \frac{\sqrt{(\lambda_1 - \lambda_2)^2 + (\lambda_1 - \lambda_3)^2 + (\lambda_2 - \lambda_3)^2}}{\lambda_1^2 + \lambda_2^2 + \lambda_3^2} \]

FA=0

FA=0.8
Acquire DWI of 831 subjects (12-22 years) on Siemens TIM TRIO and GE Discovery MR750:

- **Reverse:**
  2D Axial Spin Echo Echo-Planar - $b=0/500$, 6 directions  
  (TR=10,000, TE=85, Thick=2.5, Loc=65, FOV=240,  
  xy_matrix=96x96, Phase = A/P, Partial k-space (48/64),  
  Acceleration=2, Resolution=2.5x2.5x2.5 mm, Fat Sat=on)  
  To correct for B0 field inhomogeneity spatial distortion

- **Forward:**
  2D Axial Spin Echo Echo-Planar - $b=0/1000$, 60 directions  
  (TR=10,000, TE=85, Thick=2.5, Loc=65, FOV=240,  
  xy_matrix=96x96, Phase = A/P, Partial k-space (48/64),  
  Acceleration=2, Resolution=2.5x2.5x2.5 mm, Fat Sat=on)  
  To compute FA Maps
Archive and share data via local IT infrastructure and the Cloud
Overview

- NCANDA Data Acquisition
- DWI Specific Processing
- Current Findings (N=671)
Correct for Manufacture Differences

Normalize FA accounting for scanner differences:
• scan the same 3 human phantoms at all 5 sites
• compute ratio of mean FA value across scanner type
• apply ratio to FA maps
Tract-Based Spatial Statistics (TBSS)*

* Smith et al. 2006

Compare FA maps via TBSS Skeleton
Tract-Based Spatial Statistics (TBSS)*

[* Smith et al. 2006]*

Compute Mean Skeleton
Tract-Based Spatial Statistics (TBSS)*

* Smith et al. 2006

Compute Subject Specific Skeleton

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ROIs are defined according to JHU DTI Atlas (Mori et al. 2005)
General Additive Model (GAM)

For each ROI of the atlas regress a thin plate spline with 3 control points to the mean skeleton FA values of that region \( \text{meanFA}_{ROI} \) of the 671 subjects with the subject’s age being the predictor value and factors race, sex, and supratentorium volume (svol):

\[
\text{GAM}[ \text{meanFA}_{ROI} \sim s(\text{age, bs = "ts", k = 3}) + \text{race} + \text{sex} + \text{svol}] 
\]

**Picture**

P –value computations
Overview

- NCANDA Data Acquisition
- DWI Specific Processing
- Current Findings (N=671)
• Fiber organization peaks at 18.2 years
• African-Americans have higher and Asians have lower mean skeleton FA compared to Caucasians
Commissural Fibers

**Development of white matter fiber systems is ROI specific**

<table>
<thead>
<tr>
<th>Region</th>
<th>Adjusted Volume (cc)</th>
<th>Age (years)</th>
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<tbody>
<tr>
<td>Genu</td>
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<td>Splenium</td>
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<td>Tapetum</td>
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PROJECTION FIBERS: Brainstem Tracts

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**Superior Cerebellar Peduncle**

- Asian
- Caucasian
- Afr Amer

**Middle Cerebellar Peduncle**

- Asian
- Caucasian
- Afr Amer

**Pontine Crossing Fibers**

- Asian
- Caucasian
- Afr Amer

**Inferior Cerebellar Peduncle**

- Asian
- Caucasian
- Afr Amer

**Cerebral Peduncle**

- Asian
- Caucasian
- Afr Amer
PROJECTION FIBERS: Corticospinal Tracts (Part 2)
ASSOCIATION FIBERS: Limbic Tracts

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ASSOCIATION FIBERS: Fasciculi

Superior Longitudinal Fasciculus

Superior Frontal Occipital Fasciculus

Sagittal Striatum

Uncinate Fasciculus

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Conclusion

- Heterochronicity characterizes developmental patterns of white matter fiber systems in adolescence, e.g., commissural and selective projection systems reach peak fiber organization (assumed from FA) earlier than limbic association fibers.
- These patterns of age-related differences need confirmation with longitudinal examination.
- The continuing development of fiber bundles estimated from this cross-sectional analysis may render them vulnerable to environmental insult, including initiation of hazardous drinking.
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