What is DTI?

- **Diffusion Tensor Imaging**
- Imaging method that uses the diffusion of water to assess white matter in the brain.
Concept Behind DTI
Concept Behind DTI

Brownian Motion

Isotropy
Concept Behind DTI

Axon Bundle
Concept Behind DTI

Anisotropy

Axon Bundle

Anisotropy

Diffusion Tensor Imaging
The Diffusion Tensor

Scalar
One dimension

Vector
Two dimensions

Tensor
Three dimensions
The Diffusion Tensor

6 Directions

\[ D = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{pmatrix} \]

Eigen-values
Eigen-vectors

"Correspond to the main diffusion directions and associated diffusivities"
Le Bihan, et al., 2001
Extracting Information

- **Mean Diffusivity** (MD)
- **Overall Diffusivity**
- **Fractional Anisotropy** (FA)
- Index that reflects degree of directionality
Extracting Information

Mean Diffusivity → MD → Overall Diffusivity

Fractional Anisotropy → FA → Index that reflects degree of directionality
Extracting Information

- Mean Diffusivity
- Overall Diffusivity
- Fractional Anisotropy
- Index that reflects degree of directionality

MD

FA
Imaging (Applications)

**Brain White Matter**
- Location of axonal tracts
- White matter density
- Myelin fiber integrity

**Brain Connectivity**
- Tractography
- Characterize connections between parts of the brain.
Studies on White Matter (WM) Development
The relations between white matter and declarative memory in older children and adolescents

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$^b$Department of Psychology, University of Toronto, Toronto, Ontario, Canada
$^c$Brain-Body Institute, St. Joseph’s Healthcare, Hamilton, Ontario, Canada
$^d$Department of Electrical and Computer Engineering, School of Biomedical Engineering, McMaster University, Hamilton, Ontario, Canada
$^e$Department of Medical Physics, McMaster University, Hamilton, Ontario, Canada

**What?** - Individual Differences in WM

**In?** - Declarative Memory, Ucinate Fasciculus

**Using?** - FA Value Correlation, Probabilistic Tractography and TBSS
Their Methods

Data Analysis

- Probabilistic Tractography with FDT (for UF)
- Calculate mean FA, MD and eigen-values for ROIs
- Correlate values with age and behavioral scores
- Use TBSS for voxel-wise statistical analysis
Their Results

Table 1 – Means, standard deviations, and correlations with age and IQ across the sample for the all tasks.

<table>
<thead>
<tr>
<th>Task Description</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Correlation with age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short form estimate of IQ (Standard Score)</td>
<td>119.77</td>
<td>10.59</td>
<td>N/A</td>
</tr>
<tr>
<td>CVLT-C: Free recall composite</td>
<td>12.30</td>
<td>1.85</td>
<td>.07</td>
</tr>
<tr>
<td>CVLT-C: Cued recall composite</td>
<td>12.34</td>
<td>2.00</td>
<td>.20</td>
</tr>
<tr>
<td>Rey-O: Copy</td>
<td>33.18</td>
<td>3.69</td>
<td>.07</td>
</tr>
<tr>
<td>Rey-O: Delayed recall</td>
<td>22.48</td>
<td>6.89</td>
<td>.52 *</td>
</tr>
</tbody>
</table>

* p < .01

Correlation between age/IQ and memory
Their Results

Relations between WM and Memory in Uncinate Fasciculus

- No FA differences
- Negative Corr. with MD
- Negative Corr. with 2nd eigenvalue

Correlation between Indices and Free Recall

\[ r = -0.41, p = 0.03 \]
Their Results

Relations between WM and Memory in WM compartments

<table>
<thead>
<tr>
<th></th>
<th>FA</th>
<th>MD</th>
<th>1st</th>
<th>2nd</th>
<th>3rd</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frontal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>.46*</td>
<td>-.24</td>
<td>-.09</td>
<td>-.28</td>
<td>-.25</td>
</tr>
<tr>
<td>Left</td>
<td>.66*</td>
<td>-.25</td>
<td>-.36</td>
<td>-.33</td>
<td>-.14</td>
</tr>
<tr>
<td><strong>Parietal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>.62*</td>
<td>-.34</td>
<td>-.36</td>
<td>-.43</td>
<td>-.16</td>
</tr>
<tr>
<td>Left</td>
<td>.70*</td>
<td>-.39</td>
<td>-.03</td>
<td>-.56*</td>
<td>-.19</td>
</tr>
<tr>
<td><strong>Temporal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>.53*</td>
<td>-.37</td>
<td>-.12</td>
<td>-.58*</td>
<td>-.18</td>
</tr>
<tr>
<td>Left</td>
<td>.46*</td>
<td>-.34</td>
<td>-.09</td>
<td>-.58*</td>
<td>-.15</td>
</tr>
<tr>
<td><strong>Occipital</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>.28</td>
<td>-.33</td>
<td>-.14</td>
<td>-.41</td>
<td>-.20</td>
</tr>
<tr>
<td>Left</td>
<td>.29</td>
<td>-.39</td>
<td>-.11</td>
<td>-.45</td>
<td>-.26</td>
</tr>
<tr>
<td><strong>Posterior Fossa</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pons</td>
<td>.24</td>
<td>-.26</td>
<td>-.08</td>
<td>-.13</td>
<td>-.25</td>
</tr>
<tr>
<td>Vermis</td>
<td>.24</td>
<td>-.24</td>
<td>-.38</td>
<td>-.01</td>
<td>-.04</td>
</tr>
<tr>
<td>Right cerebellum</td>
<td>.16</td>
<td>-.39</td>
<td>-.06</td>
<td>-.44</td>
<td>-.32</td>
</tr>
<tr>
<td>Left cerebellum</td>
<td>.09</td>
<td>-.42</td>
<td>-.36</td>
<td>-.31</td>
<td>-.27</td>
</tr>
</tbody>
</table>

** p < .01.

Correlation between Indices and Age

FA increases in frontal, parietal and temporal.
Their Results

### Table 3 – Relations between FA for fiber pathways/hemispheric white matter and auditory-verbal memory accounting for IQ.

<table>
<thead>
<tr>
<th></th>
<th>Auditory-Verbal</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Free Recall</td>
<td>Cued Recall</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>FA</td>
<td>1st</td>
<td>2nd</td>
<td>3rd</td>
<td>MD</td>
<td>FA</td>
</tr>
<tr>
<td>Parietal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>.37</td>
<td>.65**</td>
<td>.12</td>
<td>-.18</td>
<td>.44</td>
<td>.52**</td>
</tr>
<tr>
<td>Left</td>
<td>.29</td>
<td>.66**</td>
<td>.20</td>
<td>-.13</td>
<td>* .58**</td>
<td>.45</td>
</tr>
<tr>
<td>Occipital</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>.17</td>
<td>.26</td>
<td>-.51**</td>
<td>-.24</td>
<td>-.34</td>
<td>.22</td>
</tr>
<tr>
<td>Posterior fossa</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left cerebellum</td>
<td>.31</td>
<td>.23</td>
<td>-.38</td>
<td>-.31</td>
<td>-.22</td>
<td>.53**</td>
</tr>
</tbody>
</table>

** p < .01.

** Positive MD correlations
### Their Results

Hierarchical Regression for Age and FA values

#### Table 5 – Hierarchical regression models predicting delayed recall of a design.

<table>
<thead>
<tr>
<th></th>
<th>Model R²</th>
<th>Model F ratio</th>
<th>Increment R²</th>
<th>Increment F ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Right Occipital</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 1:1*</td>
<td>.27</td>
<td>7.29**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Age</td>
<td>.27</td>
<td>7.29**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. FA added</td>
<td>.31</td>
<td>4.26*</td>
<td>.04</td>
<td>1.16</td>
</tr>
<tr>
<td>Model 1:2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. FA</td>
<td>.23</td>
<td>6.00**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Age added</td>
<td>.31</td>
<td>4.26*</td>
<td>.08</td>
<td>2.16</td>
</tr>
<tr>
<td><strong>Left Occipital</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 2:1</td>
<td>.27</td>
<td>7.29**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Age</td>
<td>.28</td>
<td>3.61*</td>
<td>.01</td>
<td>2.11</td>
</tr>
<tr>
<td>2. FA added</td>
<td>.28</td>
<td>3.61*</td>
<td>.01</td>
<td>2.51</td>
</tr>
<tr>
<td>Model 2:2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. FA</td>
<td>.18</td>
<td>4.38*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Age added</td>
<td>.28</td>
<td>3.61*</td>
<td>.01</td>
<td>2.51</td>
</tr>
<tr>
<td><strong>Right Temporal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 3:1</td>
<td>.27</td>
<td>7.29**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Age</td>
<td>.36</td>
<td>5.33*</td>
<td>.09</td>
<td>2.73</td>
</tr>
<tr>
<td>2. FA added</td>
<td>.36</td>
<td>5.33*</td>
<td>.08</td>
<td>2.28</td>
</tr>
<tr>
<td>Model 3:2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. FA</td>
<td>.28</td>
<td>7.87**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Age added</td>
<td>.36</td>
<td>5.33*</td>
<td>.08</td>
<td>2.28</td>
</tr>
<tr>
<td><strong>Left Temporal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 4:1</td>
<td>.27</td>
<td>7.29**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Age</td>
<td>.38</td>
<td>5.83*</td>
<td>.11</td>
<td>3.48</td>
</tr>
<tr>
<td>2. FA added</td>
<td>.38</td>
<td>5.83*</td>
<td>.09</td>
<td>2.85</td>
</tr>
</tbody>
</table>

** p < .01, * p < .05.
Their Results

Table 6 – Clusters showing significant correlations between verbal learning and FA based on TBSS.

<table>
<thead>
<tr>
<th>Cluster location</th>
<th>MNI 152 coordinates (X,Y,Z)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Free recall</strong></td>
<td></td>
</tr>
<tr>
<td>Left anterior temporal pole</td>
<td>-45, -6, -45</td>
</tr>
<tr>
<td>Right anterior temporal pole</td>
<td>46, -6, -44</td>
</tr>
<tr>
<td>Left cerebellar hemisphere</td>
<td>-36, -63, -46</td>
</tr>
<tr>
<td>Right cerebellar hemisphere</td>
<td>18, -62, -40</td>
</tr>
<tr>
<td><strong>Cued recall</strong></td>
<td></td>
</tr>
<tr>
<td>Left anterior temporal pole</td>
<td>-45, -6, -45</td>
</tr>
<tr>
<td>Right anterior temporal pole</td>
<td>46, -6, 43</td>
</tr>
<tr>
<td>Left cerebellar hemisphere</td>
<td>-30, -71, -44</td>
</tr>
<tr>
<td>Right cerebellar hemisphere</td>
<td>24, -56, -40</td>
</tr>
<tr>
<td>Brainstem</td>
<td>2, -33, -44</td>
</tr>
</tbody>
</table>
Their Results

Limitations/Considerations

- Age as a continuous variable
- IQ one SD above average
- Cross-Sectional
- No Functional Correlation

Can be addressed by using Functional ROIs
Difference:

They use radial and axial diffusivities

Radial - perpendicular to axon  
Axial - parallel to axon
Their Results

Increase in FA
Decrease in MD
Decrease in RD
Decrease in AD

-Attributed to growth of a complex microstructure and glial cells during development
White Matter Development During Childhood and Adolescence: A Cross-sectional Diffusion Tensor Imaging Study

Naama Barnea-Goraly¹, Vinod Menon¹,²,³, Mark Eckert¹, Leann Tamm⁴, Roland Bammer⁵, Asya Karchemskiy¹, Christopher C. Dant¹, and Allan L. Reiss¹

¹Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94305, USA, ²Program in Neuroscience, Stanford University, Stanford, CA 94305, USA, ³Neuroscience Institute, Stanford University, Stanford, CA 94305, USA, ⁴Department of Psychology, Children’s Hospital of Orange County, Orange, CA 92868, USA and ⁵Lucas MRS/I Center Department of Radiology, Stanford University, Stanford, CA 94305, USA

What? - WM Development

In? - Childhood/Adolescence (no behavior)

Using? - SPM, FA values
Their Results

**FA Changes with Age**
- in prefrontal regions
- within and between basal ganglia
- thalamus

**WM Density Changes with Age**
- increases in internal capsule,
  inter-thalamic pathways, and
  corpus callosum

*Figure 2. A correlation graph between FA values in sample brain regions and age. FA values were generated from two points of peak correlation between FA and age described in Table 1. (A) Right DLPFC; (B) right middle frontal gyrus.*
Difference:

They used ADC and not MD

Same thing?
Observation:

Uses SPM to correlate FA/MD with behavioral data

Doesn’t present explicit FA/MD value
Figure 1. Left: Selected sagittal slices where high FA is associated with high delay AUC. Right: Selected sagittal slices where low MD is associated with high delay AUC. Signed numbers are x-coordinates in standard MNI space.

Regions where high FA is associated with high delay
Correlation of selected FA clusters and AUC

Figure 2. Scatterplots of delay AUC-mean FA correlations for Table 2 voxel clusters.
Reviews:
- WM in Cognitive Development
- WM development as seen through DTI
  - in kids vs. adults; teens vs. adults
- Sex differences in WM development
- WM and Cognitive Function
  - IQ, working memory, information processing, reading
What we have
(Right Now)!
Example Subject - s100

Index Maps

FA

MD

1st

2nd

3rd

Eigen-Values
Example Subject - s100

Index Maps

Lines

RGB

V1 map overlaid with FA map

Greyscale
Example Subject - s100

BedpostX outputs

“bedpostx runs Markov Chain Monte Carlo sampling to build up distributions on diffusion parameters at each voxel.”

mean_f1samples - mean of distribution of FA
“PROBTRACKX involves generating connectivity distributions from user-specified seed voxel(s). All brain voxels will have a value representing the connectivity value between that voxel and the seed voxel (i.e., the number of samples that pass through that voxel).”
TBSS - Tract Based Spatial Statistics

Group 1 (4 kids) vs. Group 2 (4 adults)

1 > 2
Other Interesting Studies on DTI and Connectivity (Functional and Structural)
Amygdala tractography predicts functional connectivity and learning during feedback-guided decision-making

Michael X Cohen, a,b,c,* Christian E. Elger, a,b and Bernd Weber a,b

*a Department of Epileptology, University of Bonn, Germany
b Life & Brain Center, Department of NeuroCognition, University of Bonn, Germany
c Department of Psychology, University of California, Davis, USA

Received 9 July 2007; revised 16 September 2007; accepted 4 October 2007
Available online 12 October 2007
Development of functional and structural connectivity within the default mode network in young children

Kaustubh Supekar \textsuperscript{a,b,*}, Lucina Q. Uddin \textsuperscript{c}, Katherine Prater \textsuperscript{c}, Hitha Amin \textsuperscript{c}, Michael D. Greicius \textsuperscript{d}, Vinod Menon \textsuperscript{c,d,e,}* 

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\textsuperscript{d} Neurology and Neurological Sciences, Stanford University School of Medicine, Stanford, CA 94304, USA
\textsuperscript{e} Program in Neuroscience, Stanford University School of Medicine, Stanford, CA 94304, USA
Functionally Linked Resting-State Networks Reflect the Underlying Structural Connectivity Architecture of the Human Brain

Martijn P. van den Heuvel, René C.W. Mandl, René S. Kahn, and Hilleke E. Hulshoff Pol

Rudolf Magnus Institute of Neuroscience, University Medical Center, Utrecht, The Netherlands