Altered Hippocampal Connectivity and Midline Brain Anomalies in Children with Chromosome 22q11.2 Deletion Syndrome

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8th Biennial International 22q11.2 Deletion Syndrome Meeting
July 6-10, 2012

Hippocampus

- Important in the limbic system, involved in:
  - Memory
  - Spatial processing
  - Emotional processing
  - Linked to general intelligence level in children

Schumann, C. M. et al. (2007) Hippocampus

- Hippocampal – prefrontal functional connectivity impairments in 22q11.2DS mice model

Sigurdsson et. al. (2010) Nature

Fornix - the primary output of connections from hippocampus

Courtesy, Dr. Arthur W. Toga, Laboratory of Neuro Imaging at UCLA
Method

- Sample
  - 45 children with 22q11.2DS
  - 38 typically developing (TD) children
  - Age: 7-14 years old

- Fornix - DTI tractography
  - ROI seeding
  - probabilistic fiber-tracking (ConTrack)
  - calculate FA, RD, AD, MD

- Volume measurement
  - Cavum spetum pellucidum (CSP) & Lateral ventricles

Method - ROI Seeding in Individual Brain

Anterior seed

Posterior seed
Method - Find the Fornix Connections

- Probabilistic tractography (ConTrack)
- Calculated the most likely 100,000 connections between the front-back seeds.
- Picked the top most likely 1,000 connections (1%)

Result - Connection of Fornix

<table>
<thead>
<tr>
<th>Left Fornix</th>
<th>Type1</th>
<th>Type2</th>
</tr>
</thead>
<tbody>
<tr>
<td>from the Front Seed</td>
<td><img src="image1" alt="Connections" /></td>
<td><img src="image2" alt="Connections" /></td>
</tr>
<tr>
<td>from the Back Seed</td>
<td><img src="image3" alt="Connections" /></td>
<td><img src="image4" alt="Connections" /></td>
</tr>
<tr>
<td>“perfectly” connected</td>
<td><img src="image5" alt="Connections" /></td>
<td><img src="image6" alt="Connections" /></td>
</tr>
<tr>
<td>“tangled” with neighbor fibers</td>
<td><img src="image7" alt="Connections" /></td>
<td><img src="image8" alt="Connections" /></td>
</tr>
</tbody>
</table>
Result - Connection of Fornix

<table>
<thead>
<tr>
<th></th>
<th>Type1</th>
<th>Type2</th>
</tr>
</thead>
<tbody>
<tr>
<td>L</td>
<td>TD (n=38)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>28 (74%)</td>
<td>8 (21%)</td>
</tr>
<tr>
<td></td>
<td>&lt; 50%</td>
<td>2 (5%)</td>
</tr>
<tr>
<td></td>
<td>22q (n=45)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>21 (47%)</td>
<td>12 (27%)</td>
</tr>
<tr>
<td></td>
<td>&lt; 30%</td>
<td>6 (13%)</td>
</tr>
<tr>
<td>R</td>
<td>TD (n=38)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>24 (63%)</td>
<td>13 (34%)</td>
</tr>
<tr>
<td></td>
<td>&lt; 30%</td>
<td>1 (3%)</td>
</tr>
<tr>
<td></td>
<td>22q (n=45)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12 (27%)</td>
<td>22 (49%)</td>
</tr>
<tr>
<td></td>
<td>&lt; 30%</td>
<td>9 (20%)</td>
</tr>
</tbody>
</table>

Less organized fornix in 22q11.2DS Group
Result - Regional integrity

- Can we “zoom in” to detect where organization differs?
- anterior-posterior walk along the tract

Fractional Anisotropy Along the Trajectory
Left Fornix (Anterior to Posterior)
Right Fornix (Anterior to Posterior)

Radial Diffusivity Along the Trajectory
Left Fornix (Anterior to Posterior)
Right Fornix (Anterior to Posterior)
Result - Midline Brain Anomalies

Cavum Septum Pellucidum (CSP)

A

CSP Length in 22q11.2DS (n=79)

- 16.46%
- 32.91%
- 24.05%
- 5.08%
- 45.57%

B

CSP Length in TD (n=72)

- 26.39%
- 13.89%
- 4.17%
- 4.17%
- 55.56%

C

Cavum Septum Pellucidum Volume

- TD (n=72) - 22q (n=79)
- TD_M (n=33) - 22q_M (n=43)
- TD_F (n=39) - 22q_F (n=36)

Lateral Ventricles

Lateral Ventricular Volume

- TD (n=74) - 22q (n=80)
- TD_M (n=34) - 22q_M (n=44)
- TD_F (n=40) - 22q_F (n=36)

significant level: *** p<0.001; ** p<0.01; * p<0.05

Thursday, July 12, 12
**Result - Midline Correlations**

Lateral Ventricular Volume and Fornix

- Ventricular, **but not CSP**, volumes correlate with Fornix scalars

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**Summary**

- Atypical hippocampal connections in children with 22q11.2DS
  - less organized fornix
  - especially at the area connecting to hippocampus
  - varies a lot between children with 22q11.2DS

- Atypical **midline** structures
  - enlarged CSP
  - enlarged lateral ventricles
  - varies a lot between children with 22q11.2DS
  - *may* influence the hippocampal connections

- Not yet found strong functional implications from any single component, **BUT** each of them has been commonly reported in patients with schizophrenia.
Thanks!

All participants and their families!!

Tony Simon & the CABIL team
Naomi Goodrich-Hunsaker
Margarita Cabaral
David G. Amaral
Michael Buonocore
Danielle Harvey
Kristopher Kalish
Owen Carmichael
Yuen Ting Chan, Erica

Brian A. Wandell
Robert F. Dougherty
Michael Perry
& the Stanford University Vista Lab

http://white.stanford.edu/index.php