BRAIN STRUCTURE IN MYOTONIC DYSTROPHY TYPE 1 (DM1)

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Outline

- Iowa DM1 Brain Research Study
- Lesson on brain anatomy
- How does DM1 affect the brain?
- Does this change over time?
Iowa DM1 Brain Study

- Paid for by the National Institutes of Health (NIH)
- Began in September 2015 (though a small group participated before that as a ‘pilot sample’)
- We study brain structure (how it is put together; looking at parts) using Magnetic Resonance Imaging (MRI)
- We study brain function (how it works) using tests of thinking skills (memory, concentration, language)
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THE HUMAN BRAIN
Brain Cell = Neuron

- Brain works by billions of cells talking to each other
- **Dendrites** – communication with other neurons
- **Cell Body** – where all of the functions happen – metabolism
- **Axon** – sends electrical impulses across long distances (electrical cable)
- **Synapse** – communications between cells through exchange of neurotransmitters (brain chemicals)
THE HUMAN BRAIN
Magnetic Resonance Imaging (MRI)

Gray Matter
- Where the cell bodies are

Cerebral spinal fluid (CSF)
- Surrounds the brain and fills internal cavities

White matter
- Where the axons are (electrical cables)
- Coating on the axons is called MYELIN
How do we “measure” white matter

- We can detect ‘lesions’ in the white matter
- Places where myelin has been ‘stripped’
How do we “measure” white matter

- White Matter is made of organized tracks of fibers
  - Kind of like roads
- We can measure how straight the fibers are
  - Straight roads are better
- Called diffusion tensor imaging (DTI)
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In DM1, the White Matter is Affected Most

- DM1 patients have more white matter lesions than controls that are matched by sex and age
  - Control scan in Yellow box
  - Patient scan in red box
In DM1, the White Matter is Affected Most

- **DTI Measure**
  - Higher means straighter white matter fibers
  - Higher is BETTER
- **DM1 subjects have lower DTI measures than controls**

*ANCOVA controlling for age, F= 32.58, p<0.0001*
What is affected by changes in brain white matter?

- Thinking skills
- DTI Measure
  - How ‘straight’ the ‘roads’ are in your white matter
- The lower the DTI measure, the lower the thinking skills score

*Pearson for age, $r = 0.788$, $p<0.0001$
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Does the White Matter get less healthy over time?

- We divided our research participants into groups, based upon how long they had symptoms of DM1.
- Disease duration – determined by the age at which symptoms first started (not age of diagnosis)

<table>
<thead>
<tr>
<th>Group</th>
<th>Duration of Disease (DD)</th>
<th>N</th>
<th>Age Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Not applicable</td>
<td>15</td>
<td>47.7</td>
</tr>
<tr>
<td>Group 1 (DD short)</td>
<td>1.87 (0 – 4.4)</td>
<td>8</td>
<td>37.0</td>
</tr>
<tr>
<td>Group 2 (DD medium)</td>
<td>10.01 (6.3 – 15.2)</td>
<td>8</td>
<td>53.3</td>
</tr>
<tr>
<td>Group 3 (DD long)</td>
<td>22.7 (19.0 – 25.4)</td>
<td>8</td>
<td>43.9</td>
</tr>
</tbody>
</table>
Does the White Matter get less healthy over time?

- Even patients VERY early in the disease have decreased DTI measure
- The longer the disease, the lower the measure
Take-Home Message

- These measures of brain structure and function are consistent with what we observe and what patients/families tell us in clinic.

- Knowing the specifics of how DM1 affects the brain can help researchers develop better-targeted treatments and can help clinicians track change and determine the effects of such treatments.

- Even though DM1 may bring about various challenges, clinicians, patients and families can work together to compensate for many of the difficulties that arise.
Thank You!

Research participants – We couldn’t do this without you!

**Research Team**

Neurology: Laurie Guttmann, Cheryl Smith
Genetic Counseling: Janel Phetteplace
Research Coordinators: Stephen Cross, Claire Johnson
Postdoctoral Fellow: Ian DeVolder
Imaging: Vince Magnotta, Hans Johnson, Eric Axelson, Joel Bruss
Psychiatry: Peg Nopoulos, David Moser
Statistics: Jeff Long
Come see us in Iowa!