BRAIN STRUCTURE IN MYOTONIC DYSTROPHY TYPE 1 (DM1)

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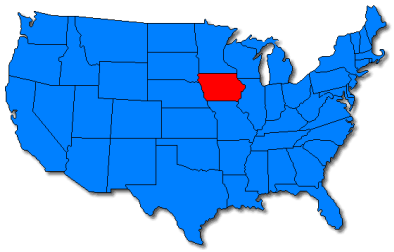
THE IOWA DM1 BRAIN STUDY TEAM
UNIVERSITY OF IOWA, IOWA CITY, IA

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')

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Brain Study

- We study brain <u>structure</u> (how it is put together; looking at parts) using Magnetic Resonance Imaging (MRI)
- We study brain <u>function</u> (how it works) using tests of thinking skills (memory, concentration, language)

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THE HUMAN BRAIN

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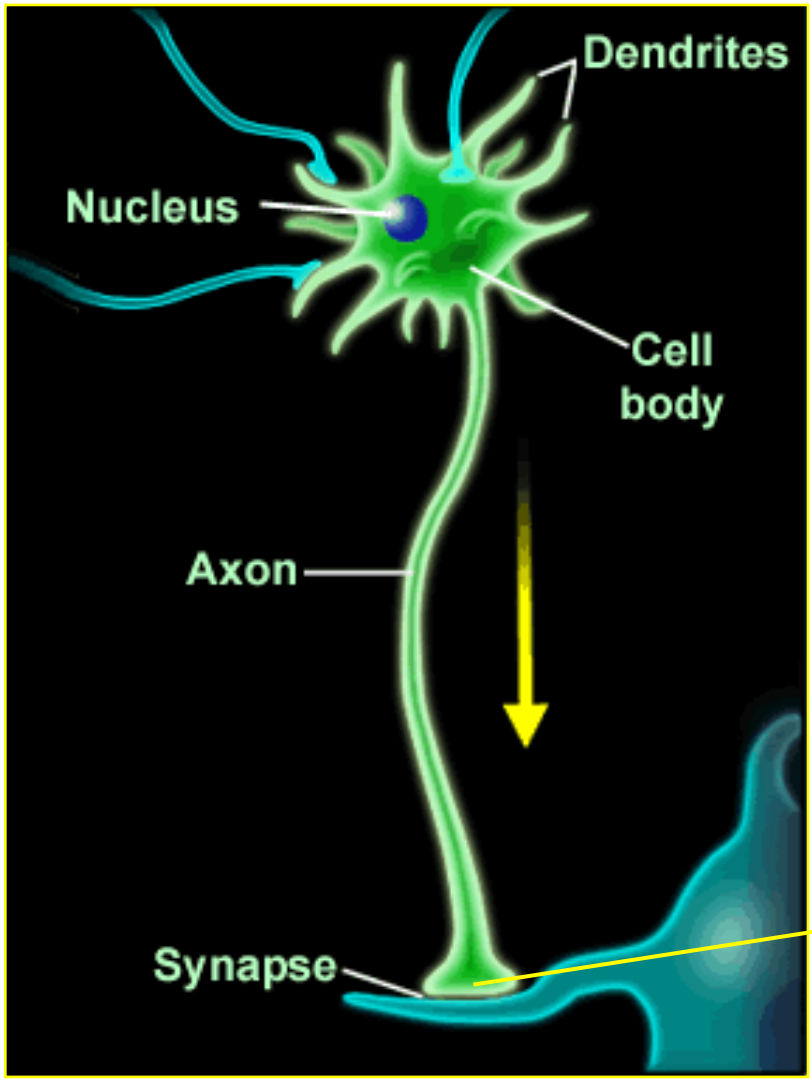
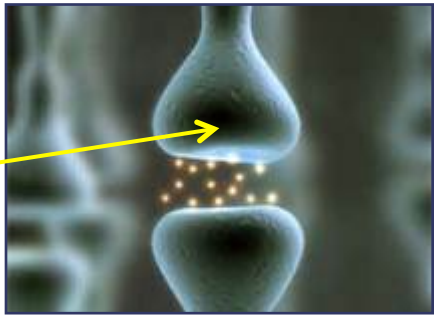


Brain Cell = Neuron

- 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)



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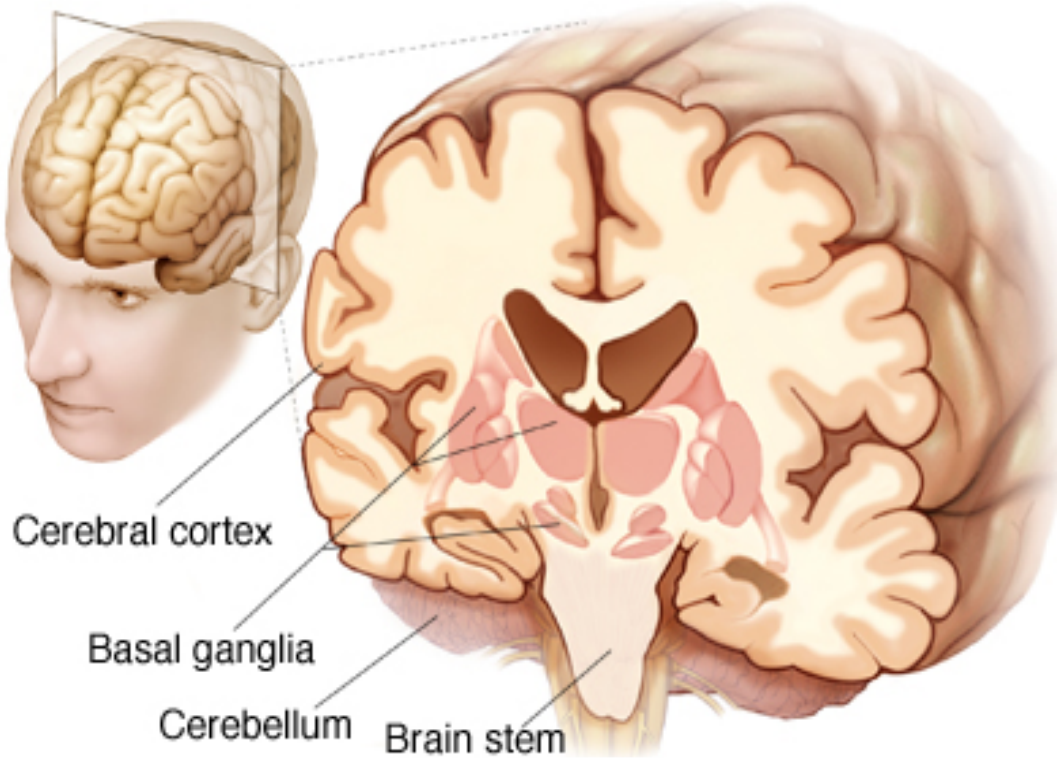

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Magnetic Resonance Imaging (MRI

Gray Matter

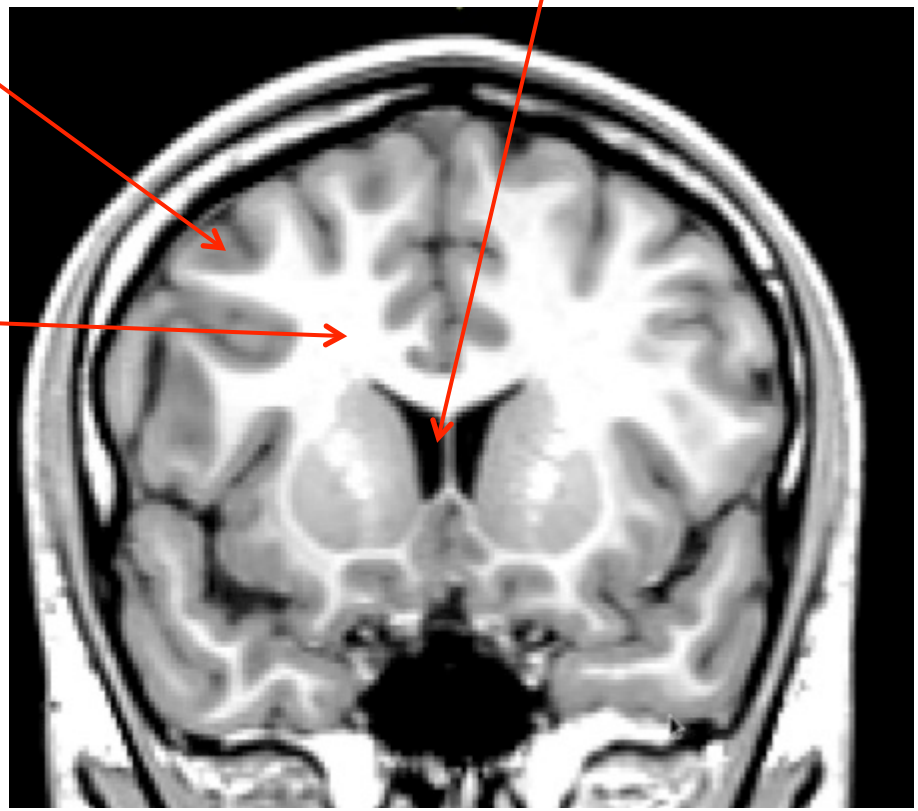
- Where the cell bodies are

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**



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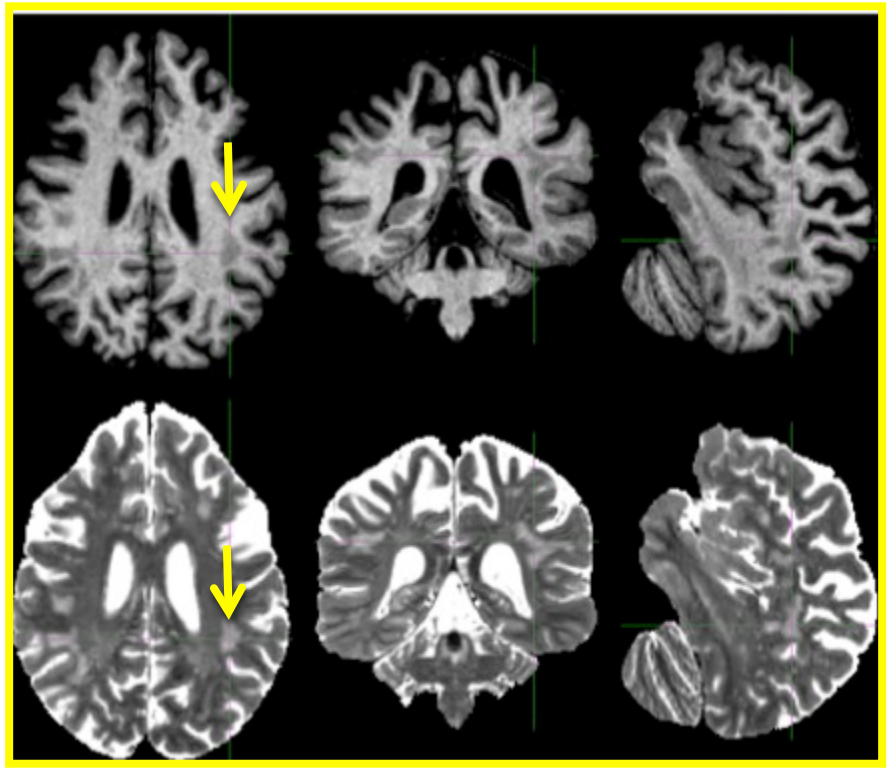
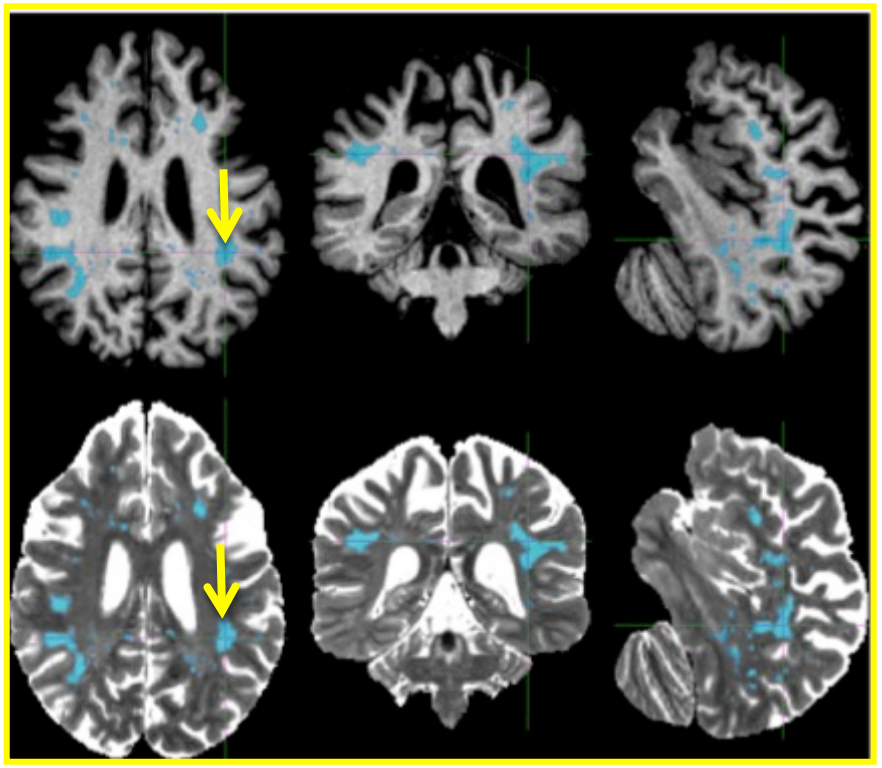
How do we “measure” white matter

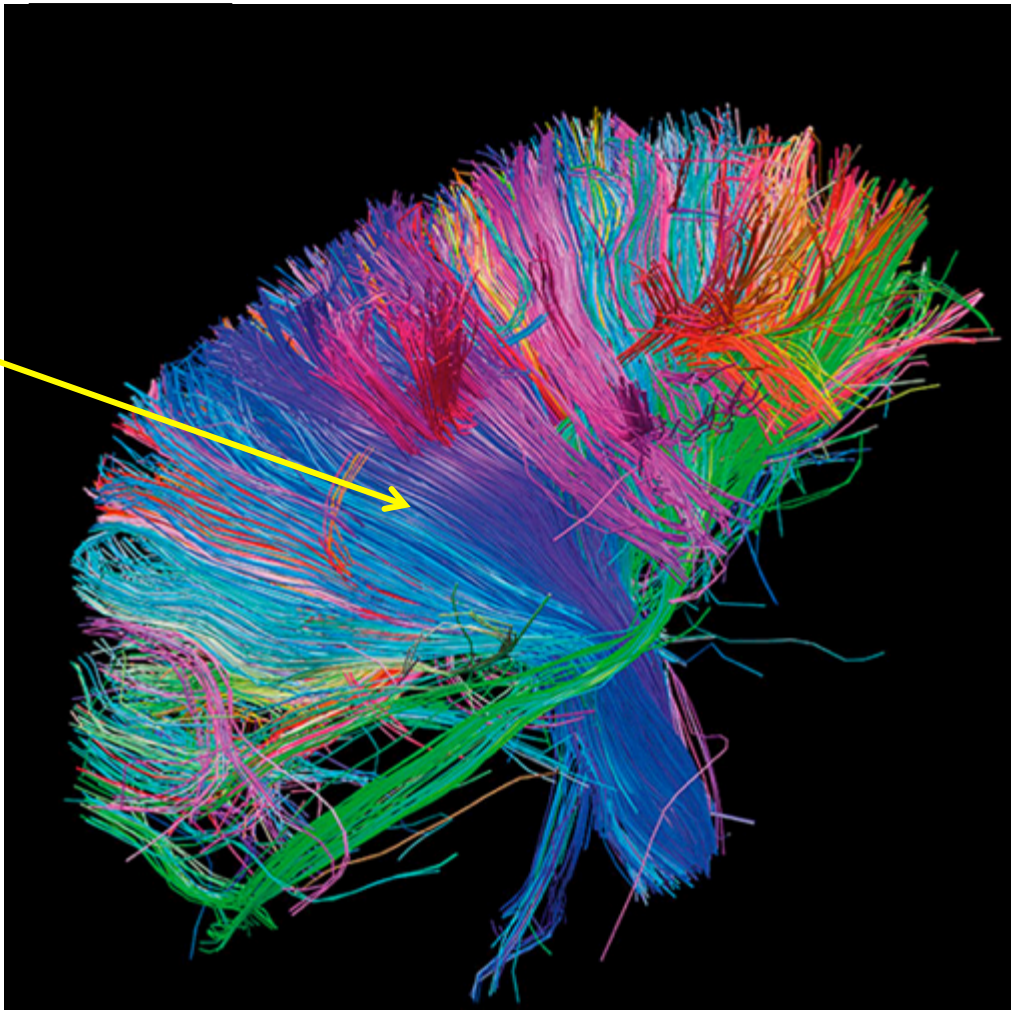
- We can detect ‘lesions’ in the white matter
- Places where myelin has been ‘stripped’





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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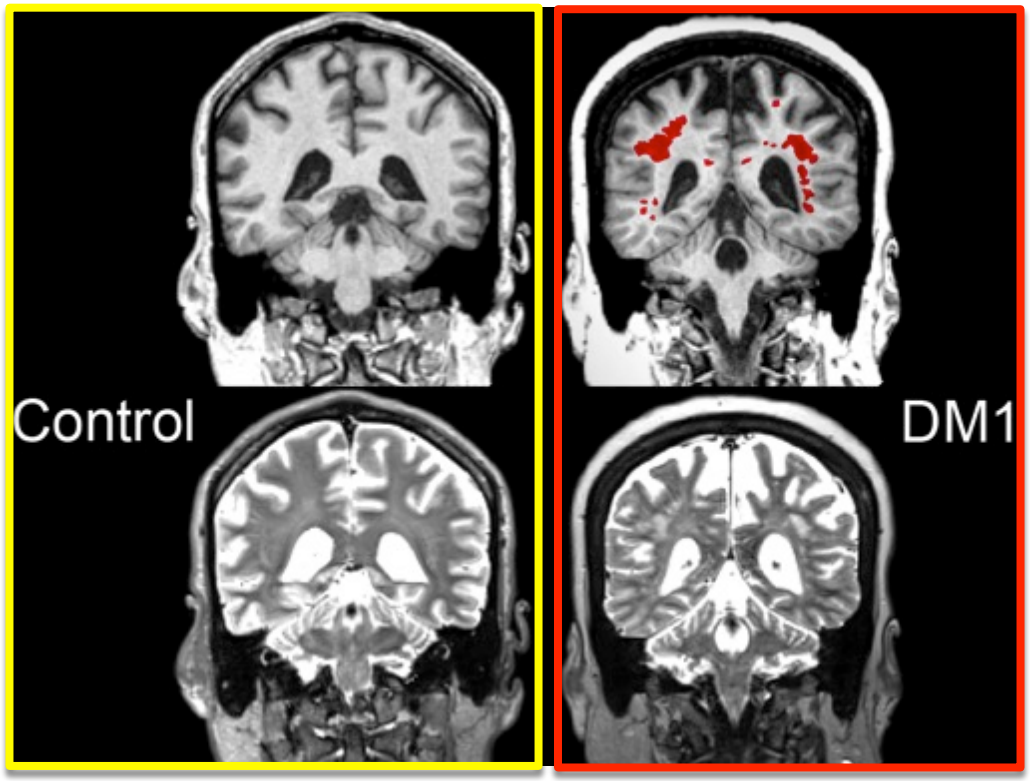
In DM1, the White Matter is Affected Most



- 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

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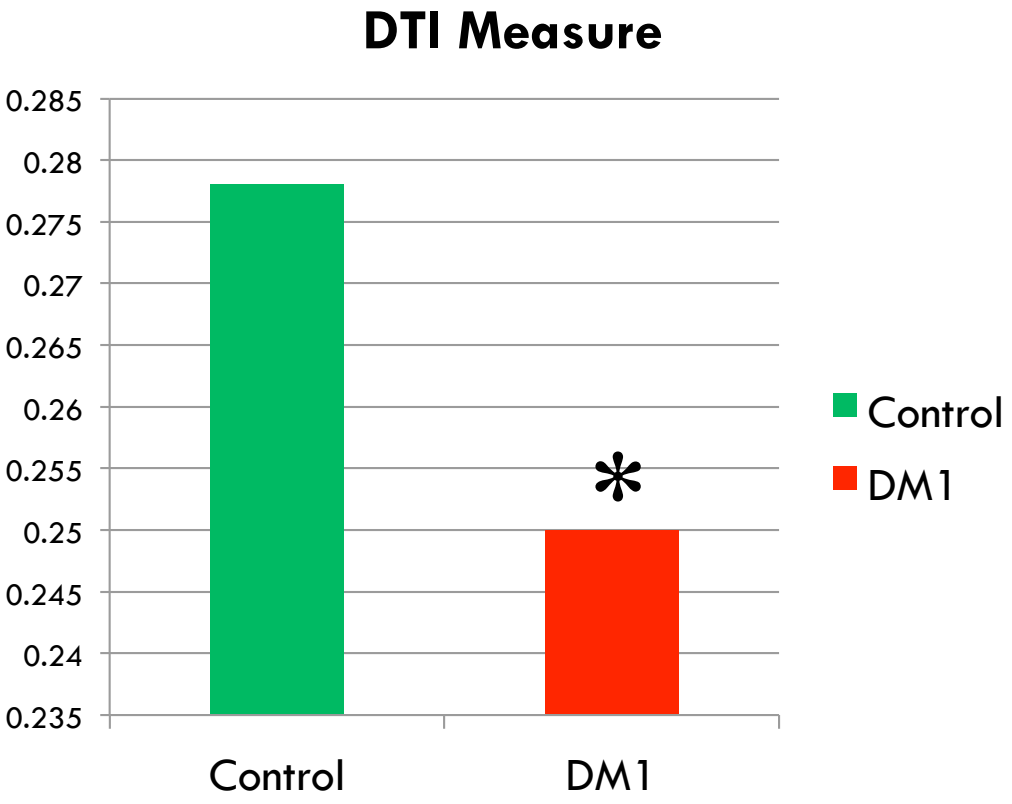
In DM1, the White Matter is Affected Most

- DTI Measure
  - Higher means straighter white matter fibers
  - Higher is BETTER
- DM1 subjects have lower DT1 measures than controls



*ANCOVA controlling for age, F= 32.58, p<0.0001

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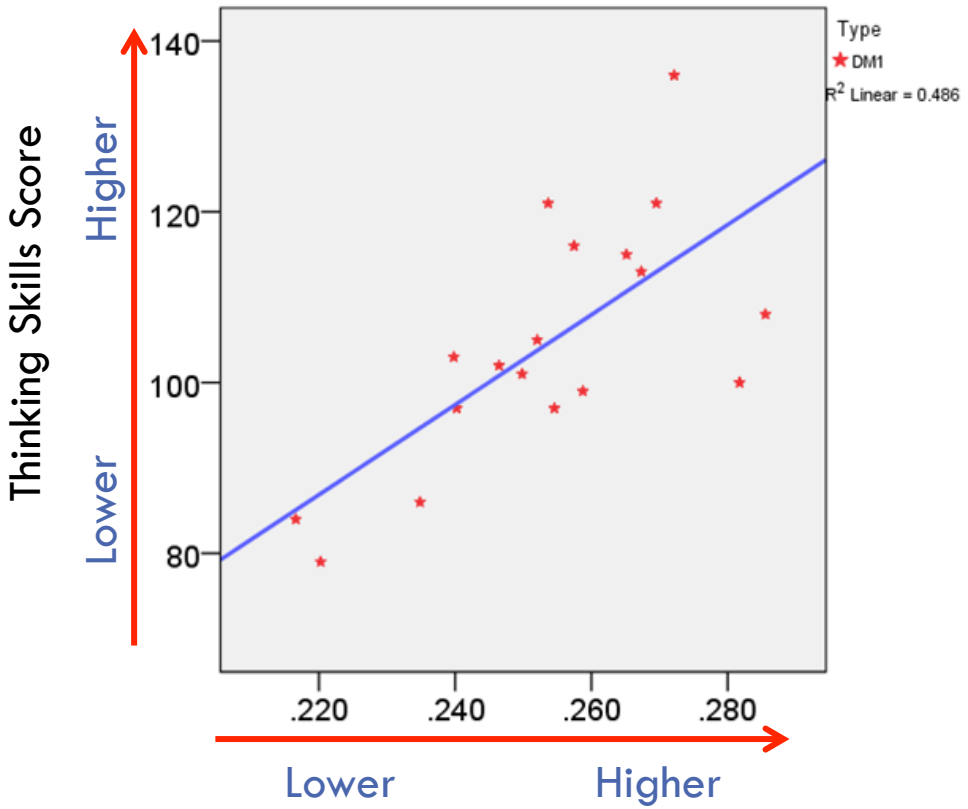
What is affected by changes in brain white matter?

- 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

The University of Iowa Myotonic Dystrophy Brain Study

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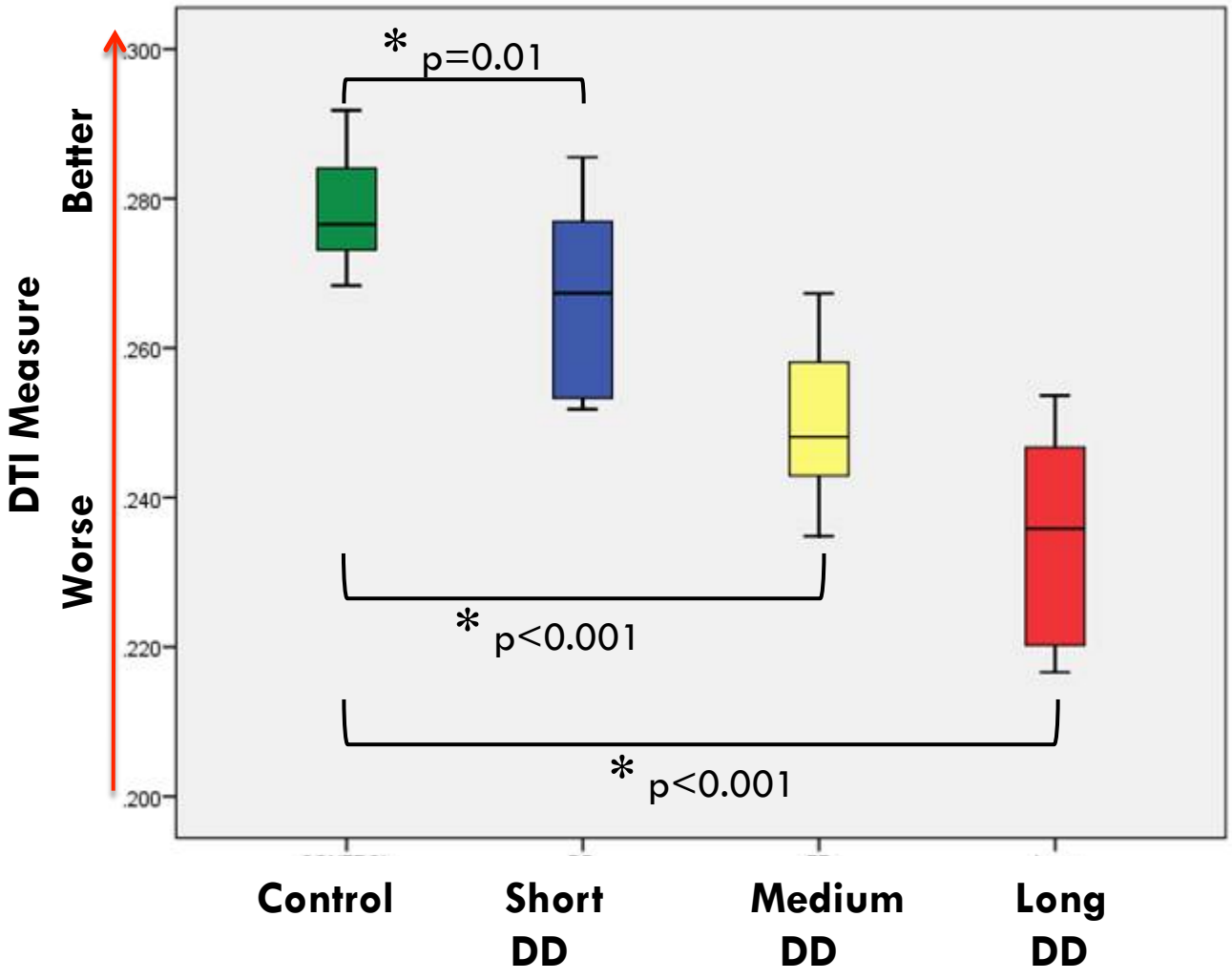
Does the White Matter get less healthy over time?

- 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)

Group	Duration of Disease (DD) Mean (range)	N	Age Mean
Control	Not applicable	15	47.7
Group 1 (DD short)	1.87 (0 – 4.4)	8	37.0
Group 2 (DD medium)	10.01 (6.3 – 15.2)	8	53.3
Group 3 (DD long)	22.7 (19.0 – 25.4)	8	43.9

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!