Advances in Understanding Neuropsychological Bases of Dyslexia

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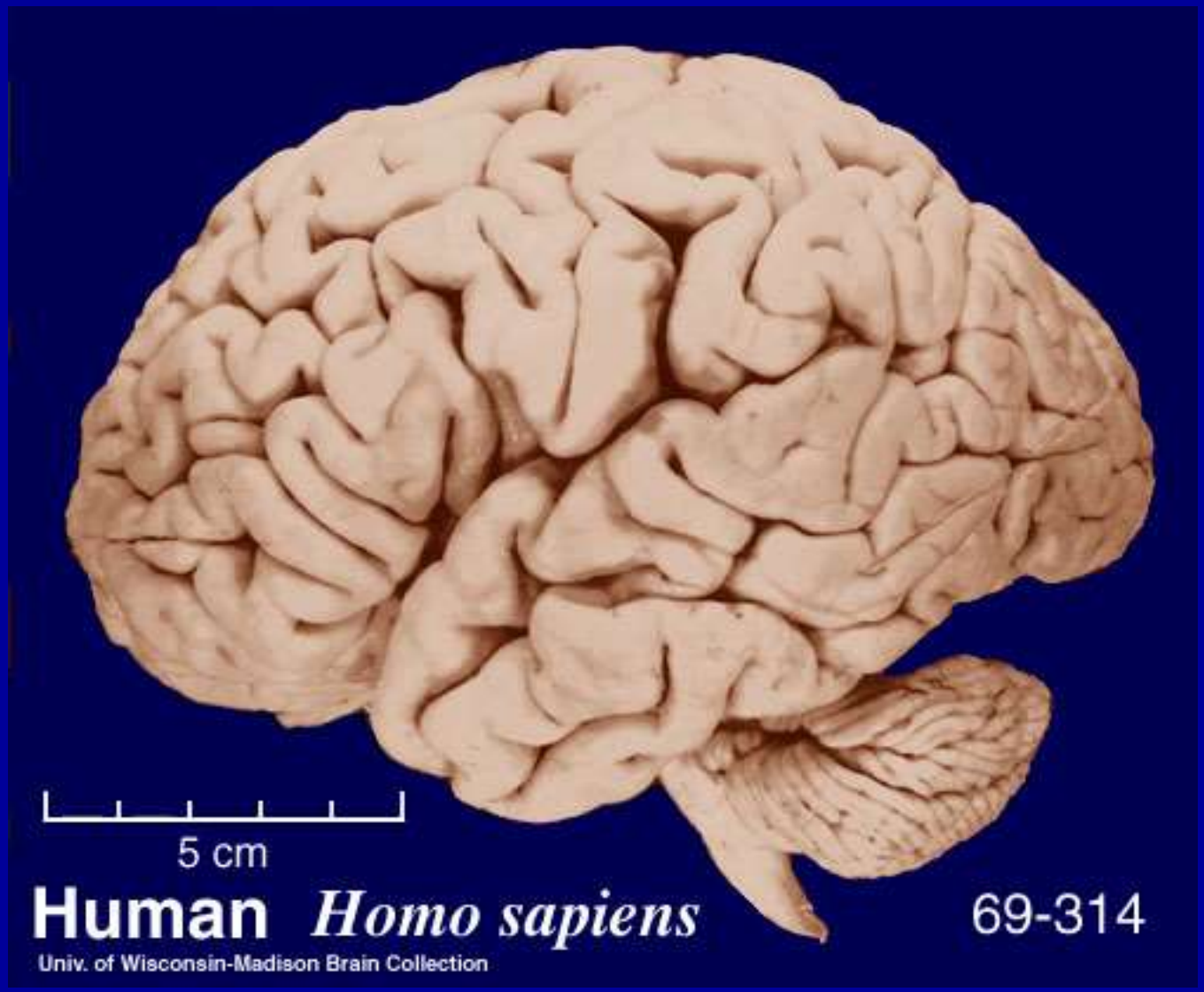
Fragile Power of the Human Brain







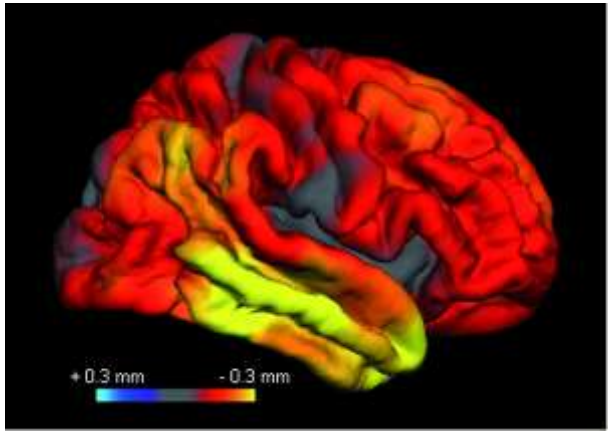




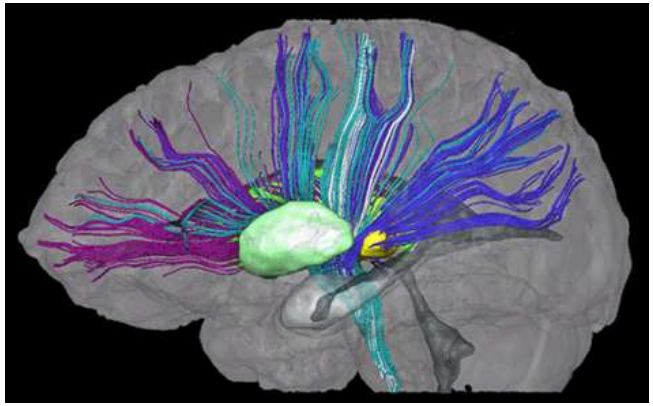
Neurodevelopmental Lottery

- **Dyslexia – 5-17% of children**
- **ADHD – 11% of children**
- **Autism/ASD – 1.5% of children (1/68; 1/42 boys)**
- **Education – 1/8 children receive special education**
- **Poverty – 21% of US children under 18**
- **Free/Reduced-priced lunches – 50% in public schools**

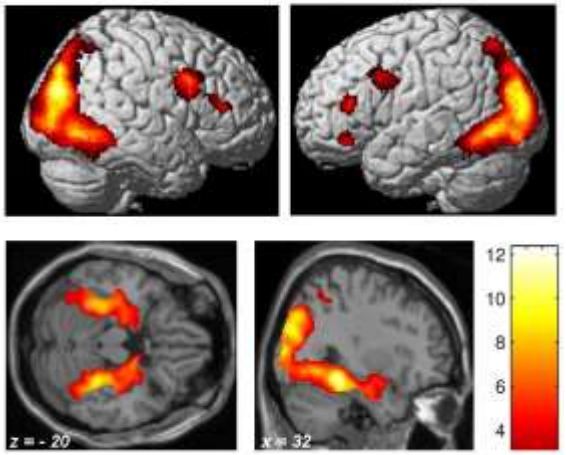
Neuroimaging



grey matter structure (MRI)



white matter structure (DTI)



grey matter function (fMRI)

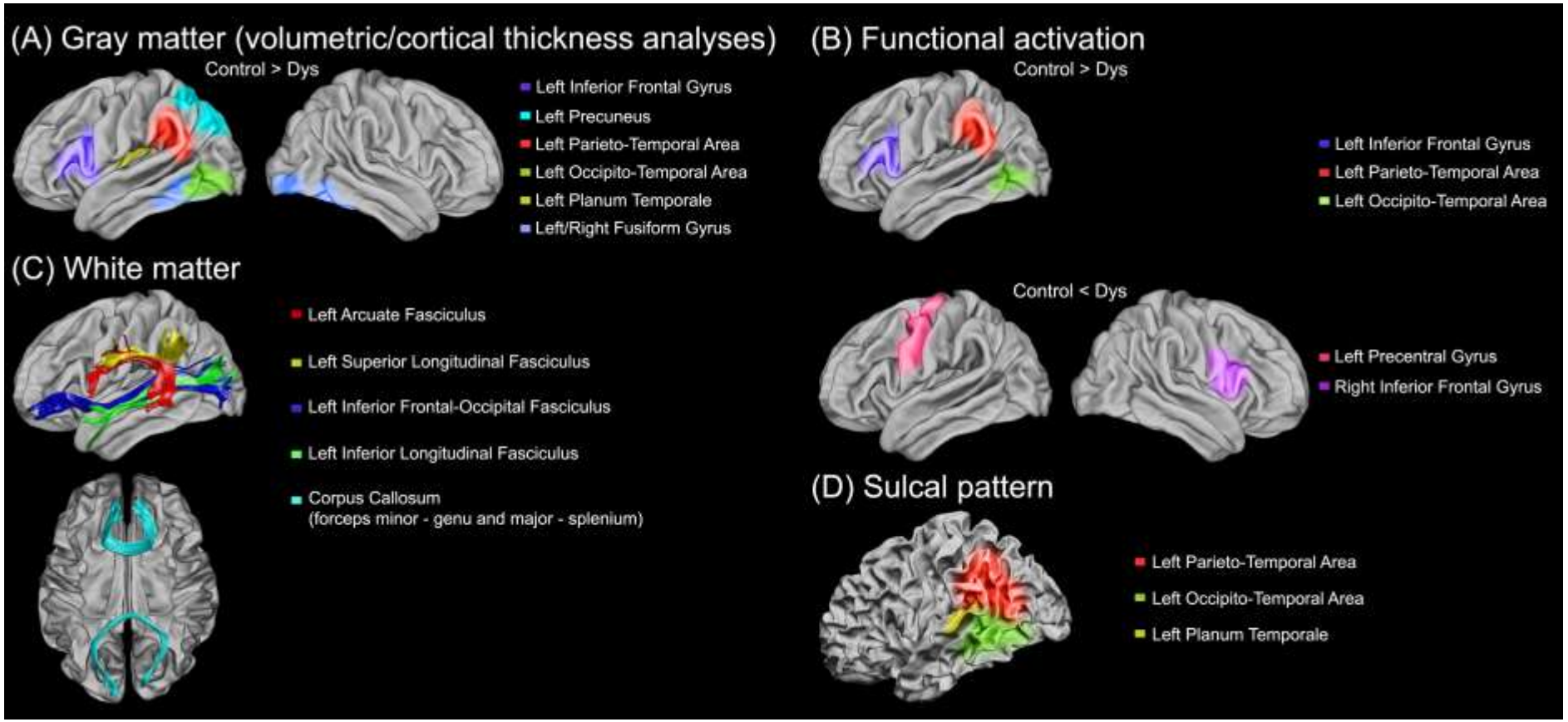
DEVELOPMENTAL DYSLEXIA

- **unexplained difficulty in reading in 5 to 17% of children**

Advances in Understanding Neuropsychological Bases of Dyslexia

- consistent brain differences in dyslexia
- brain differences in dyslexia present *before* learning to read in school
- neurophysiological differences that may lead to dyslexia
- predicting improvement in dyslexia
- variation in response to intervention

Common Structural & Functional Brain Differences in Dyslexia



Oznerov-Palchik al., *Current Opinion in Behavioral Science*, 2016

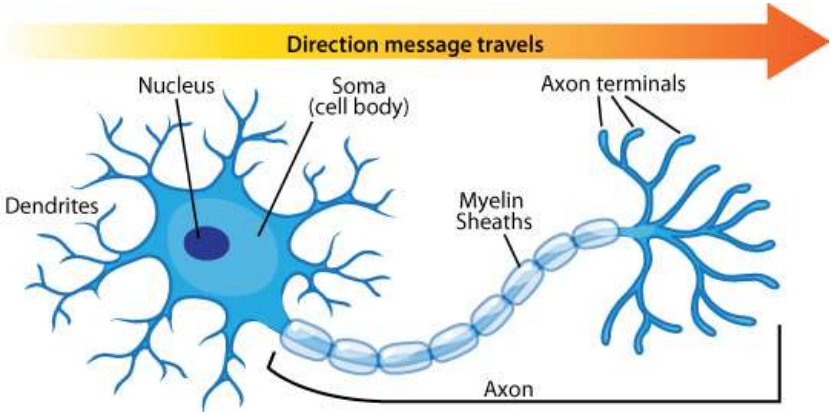
DYSLEXIA: CAUSES

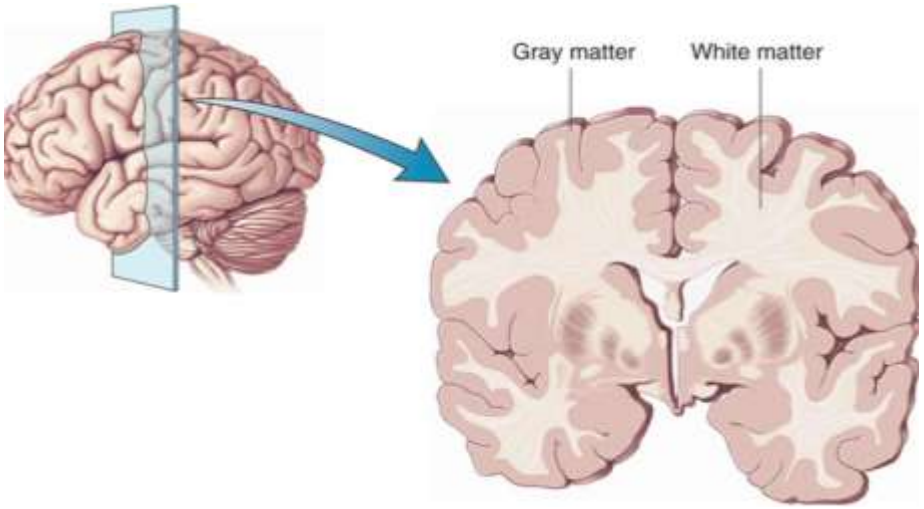
- **Phonological Hypothesis**

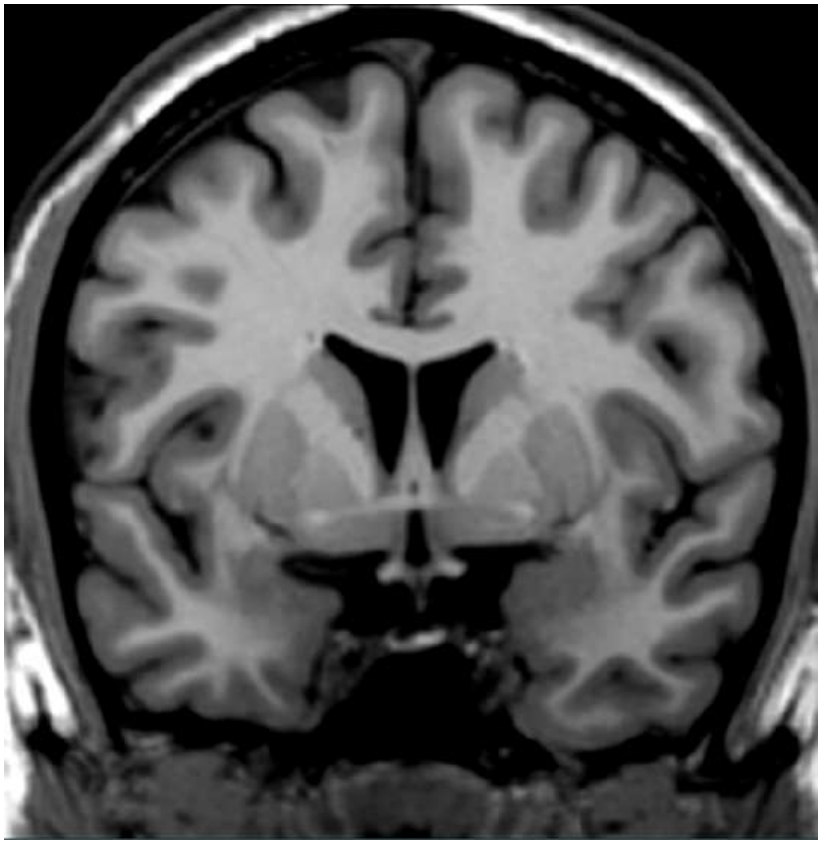
  deficit in processing of speech sounds

  poor grapheme-phoneme mapping
- **also *fluency***
- **perceptual bases (more debated)**

Grey Matter = Cell Bodies
White Matter = Myelinated Axons



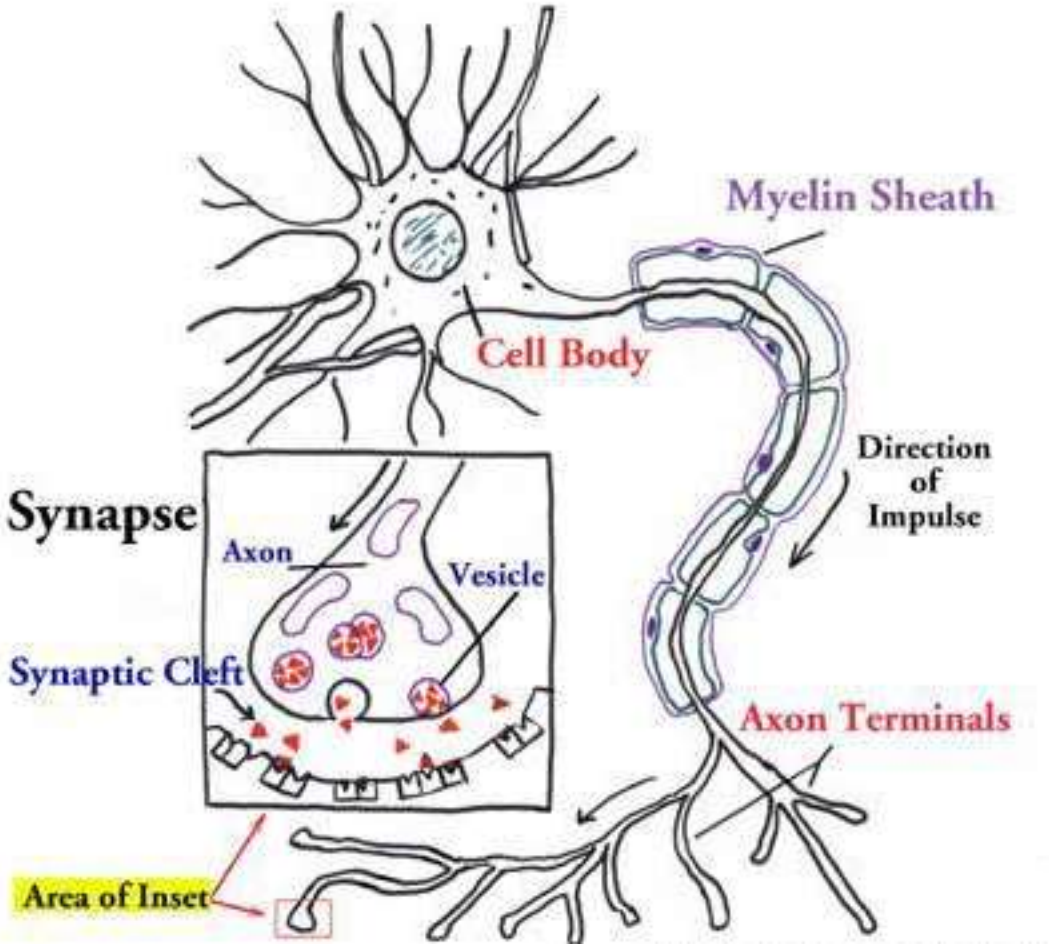




Diffusion Tensor Imaging (DTI)

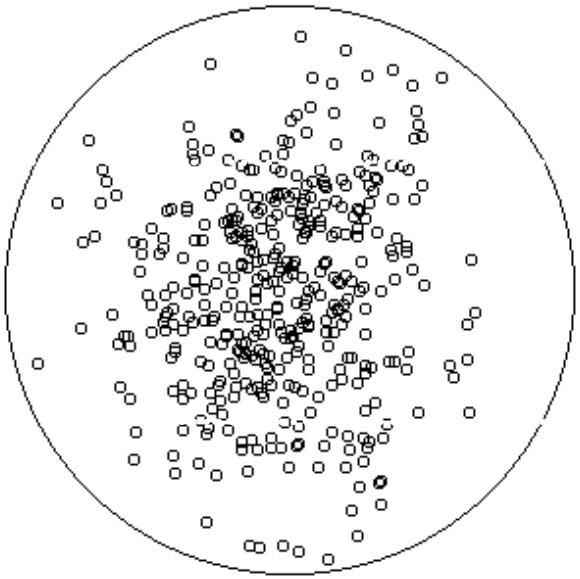
- visualizes white matter connectivity in the brain
- measures movement of water at microstructural level (microns)

NERVE AXON

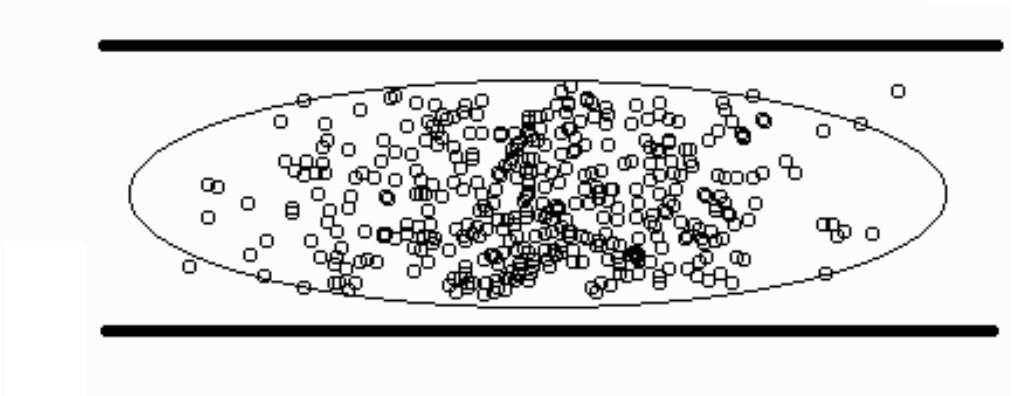

Myelin Sheath
Cell Body
Direction of Impulse
Synapse
Axon
Vesicle
Synaptic Cleft
Axon Terminals
Area of Inset

Diffusion anisotropy: Effects of myelination

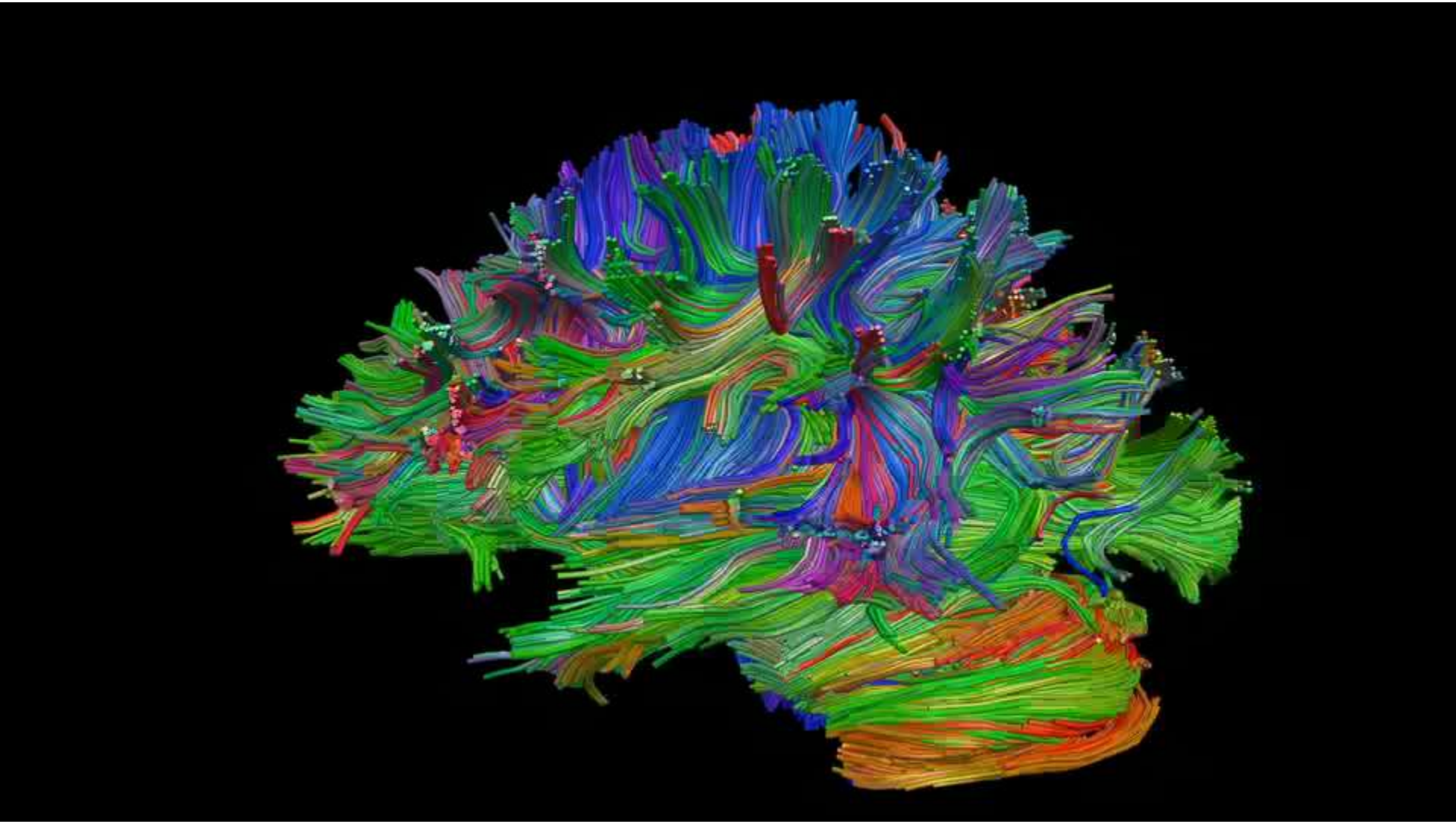
Weak/no myelin barrier



Strong myelin barrier

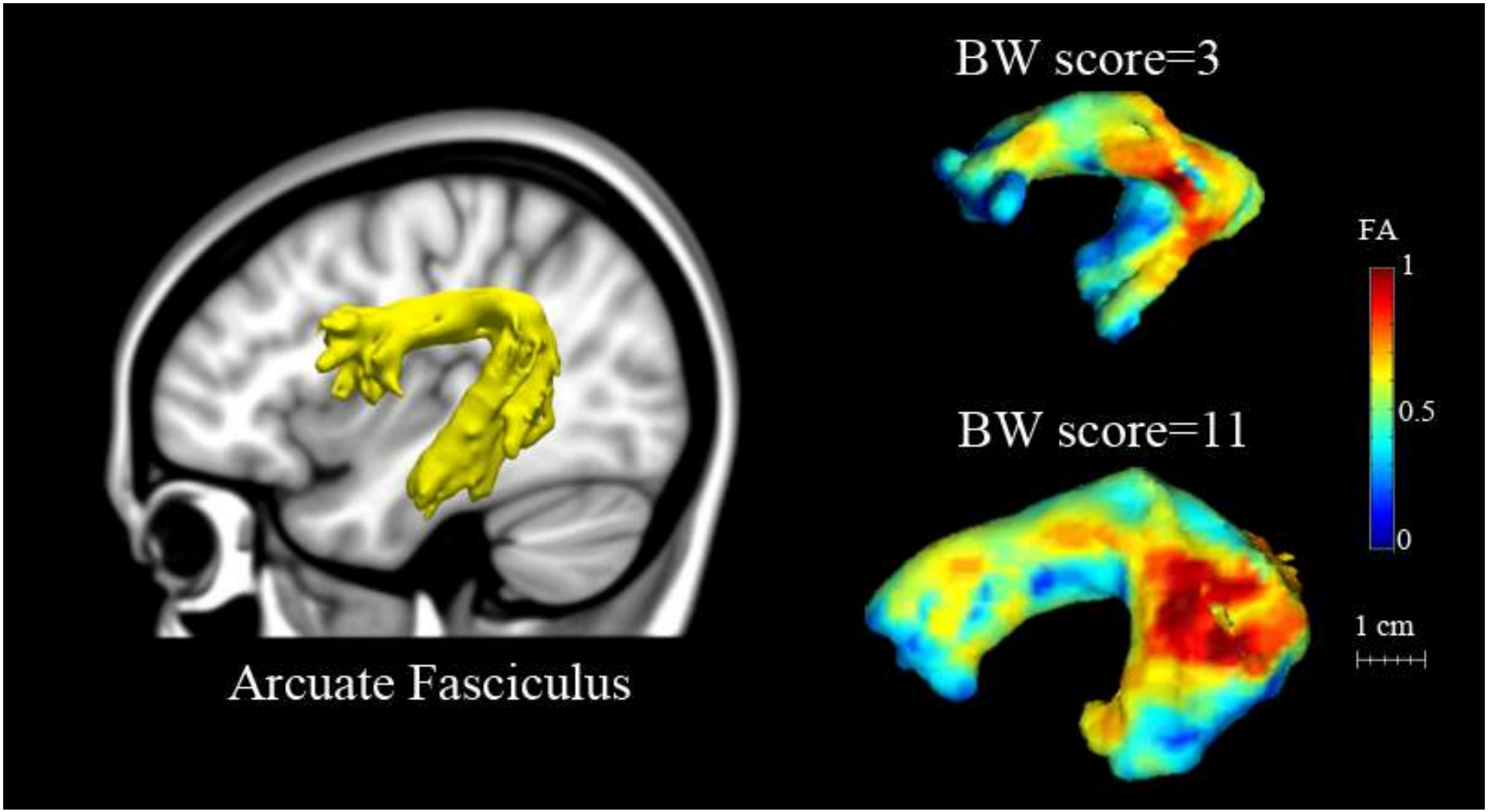


Diffusion Tensor Imaging (DTI) – Tractography



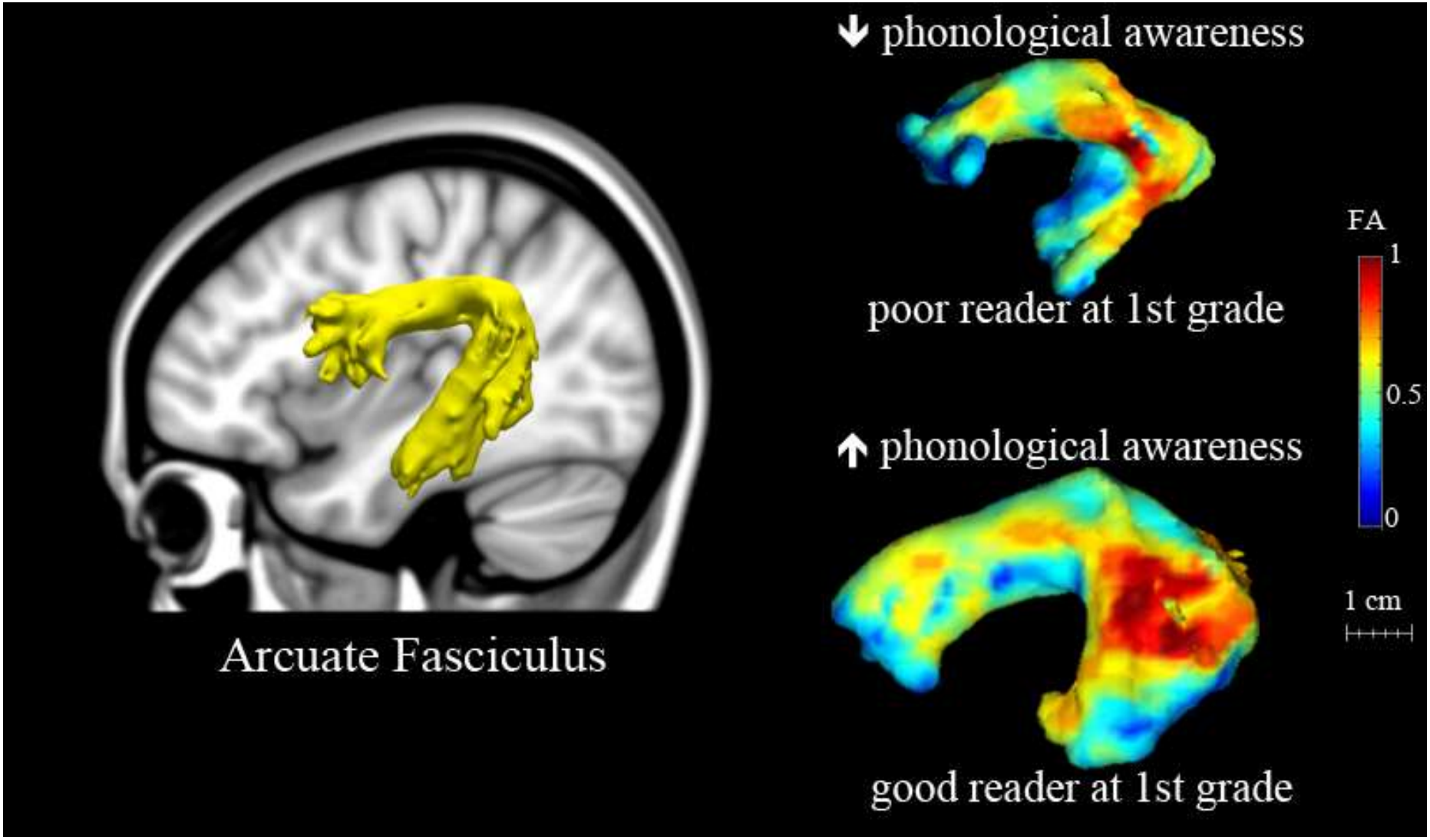
red = left-right; blue = up-down; green = front-back

Brains Better or Worse Designed for Learning to Read?



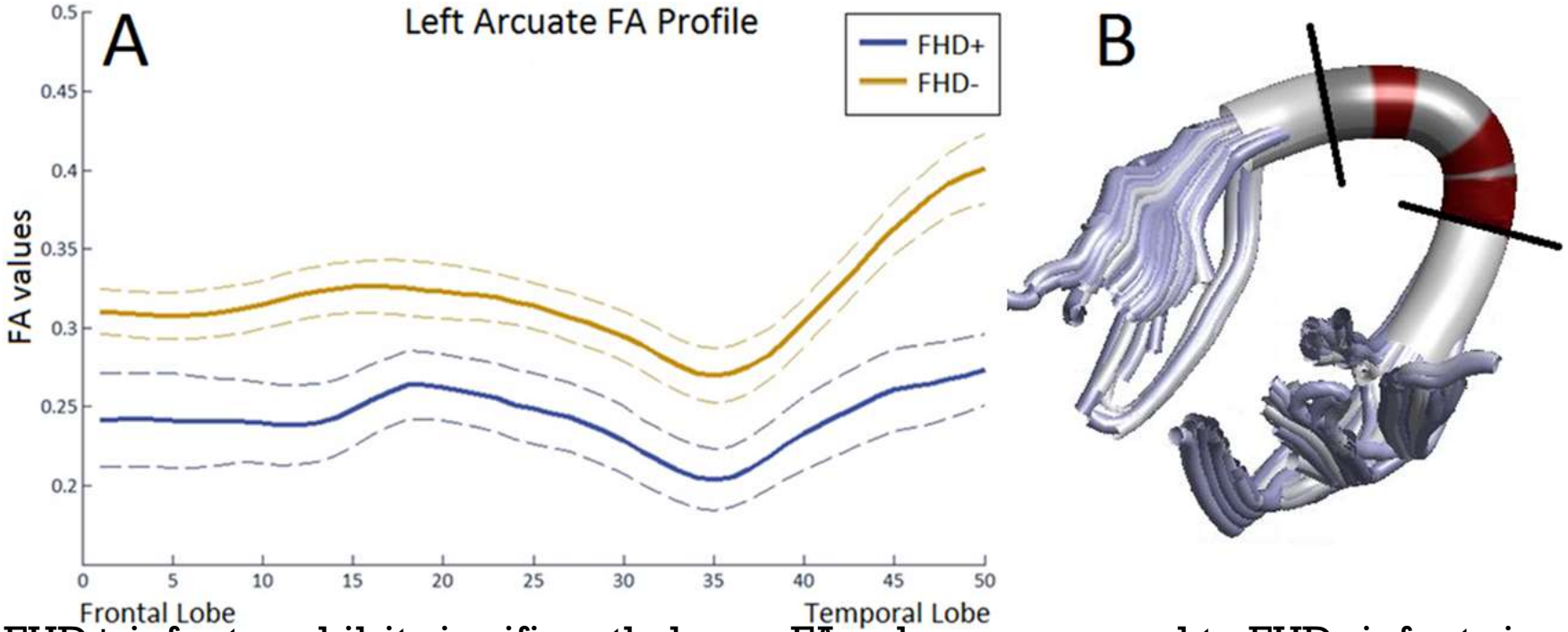
blending words (BW) - synthesize sounds to form word
(what word do these sounds make? *ham er*)

Brains Better or Worse Designed for Learning to Read?



White Matter Alterations in Infants at Risk for Developmental Dyslexia

Nicolas Langer[1,3,†], Barbara Peysakhovich[1,†], Jennifer Zuk[1,3], Marie Drottar[2], Danielle D. Sliva[1,2], Sara Smith[1], Bryce L. C. Becker[1], P. Ellen Grant[2,3] and Nadine Gaab[1,3,4]



FHD+ infants exhibit significantly lower FA values compared to FHD- infants in red regions (all $p < 0.02$, controlled for multiple comparisons)

Multivariate pattern analysis (MVPA):

MVPA (using FA at each node of the left AF as input) was performed to determine whether FA can distinguish FHD+ and FHD- infants

- 82% prediction accuracy ($p = 0.001$)

Langer *et al.*, 2015

Different Responses to Language Sounds in Infants with Family History of Dyslexia

Guttorm et al., 2001; 2005; Molfese et al., 2000

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What Leads to Difficulty in Phonological Awareness?

Hierogliphys – 3200 BC

Gutenberg Bible – Printing Press – 1450s

Brain Adaptation/Plasticity

- **when a person sees or hears a stimulus repeatedly, brain responses are reduced even as performance becomes faster**
- **reduced brain response = brain change or *plasticity* that makes perception easier, faster**

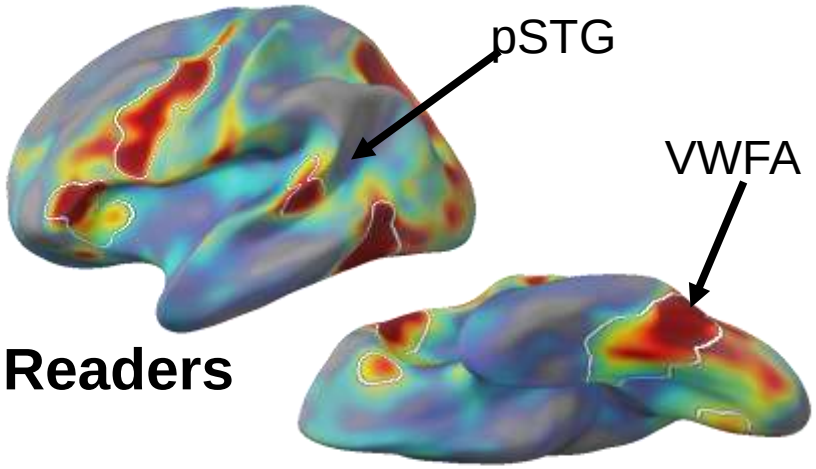
Brain Adaptation/Plasticity Difference in Dyslexia

Hypotheses

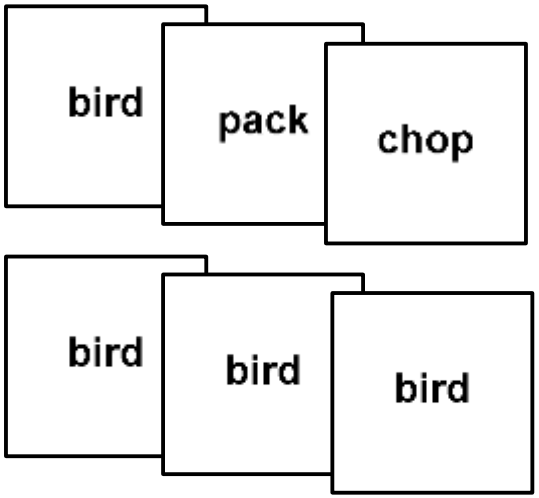
- **Print – Yes – Reading Difficulty**
- **Spoken Words – Yes – Language Difficulty**

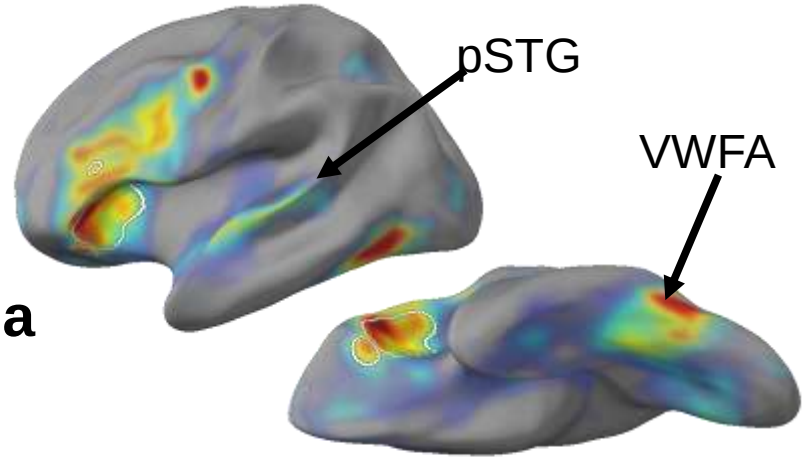
- **Objects – No – no language/reading (name)**
- **Faces – No – no language/reading**

... reduced adaptation for written words

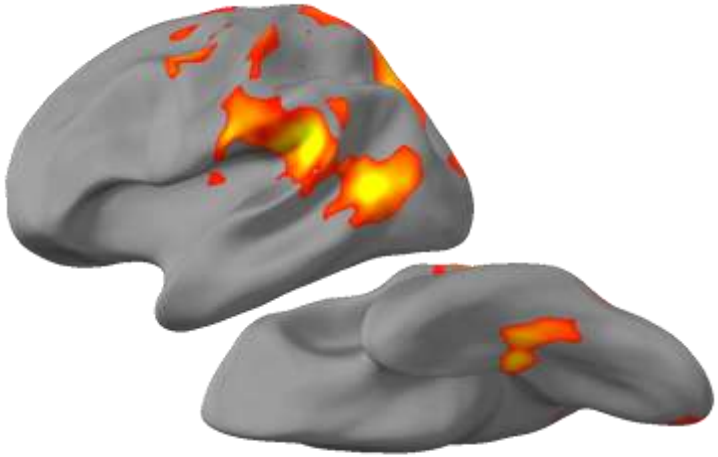


Typical Readers





Dyslexia

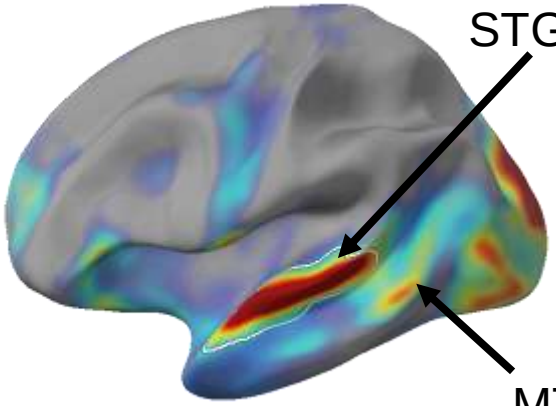


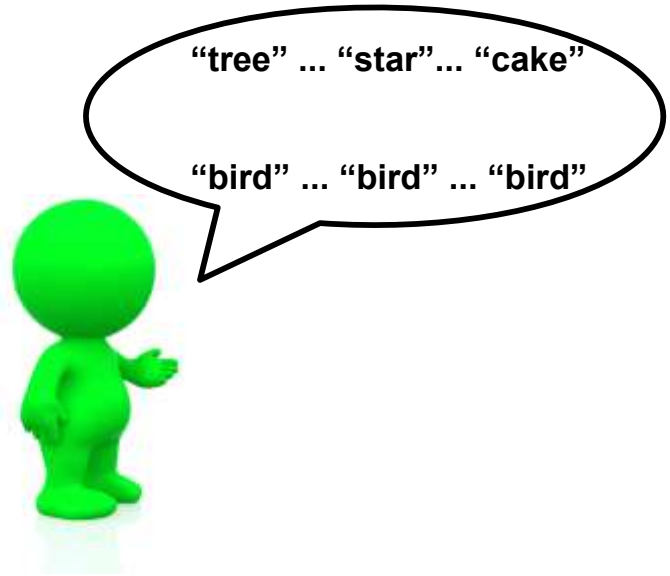
Group Difference

Perrachione *et al*. (2016) *Neuron*

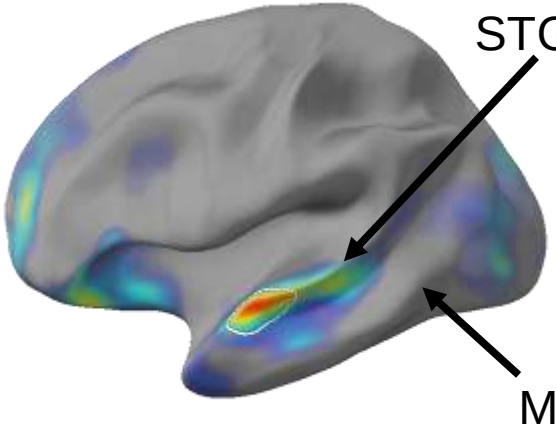
...reduced adaptation for spoken words

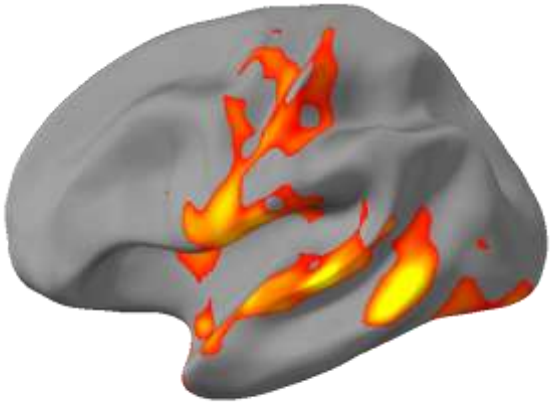
Typical Readers





Dyslexia



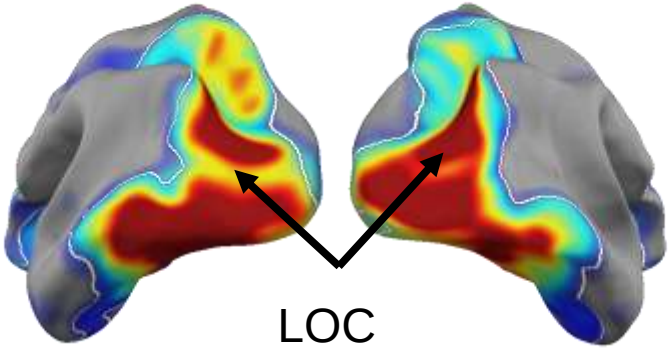


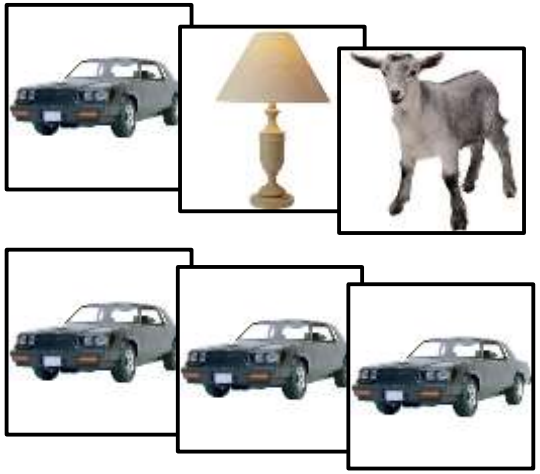
Group Difference

Perrachione *et al*. (2016) *Neuron*

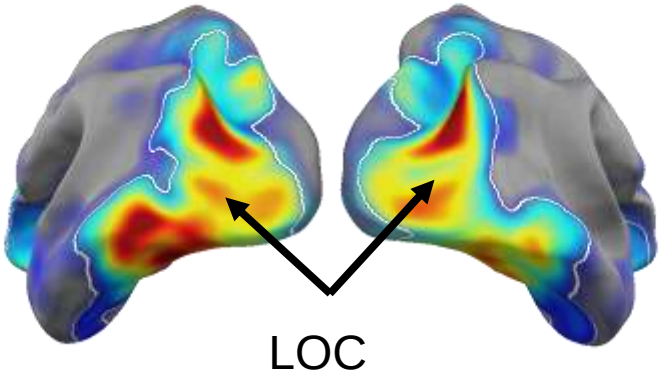
... reduced adaptation for visual objects

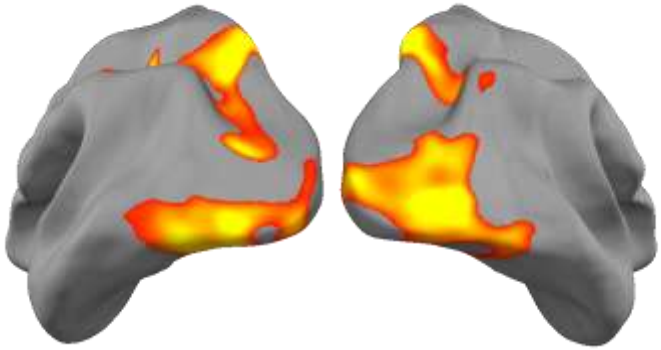
Typical Readers





Dyslexia



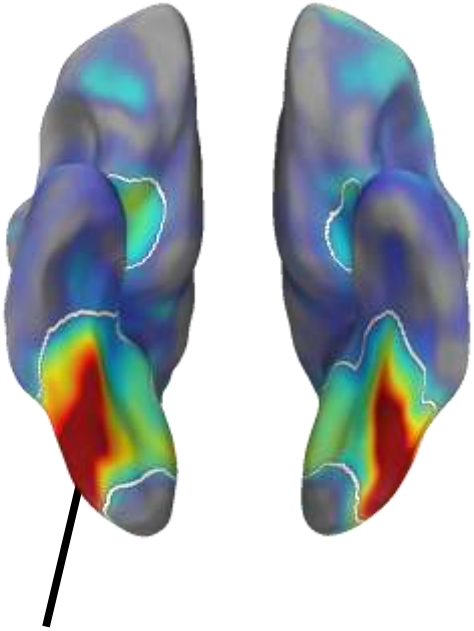


Group Difference

Perrachione *et al*. (2016) *Neuron*

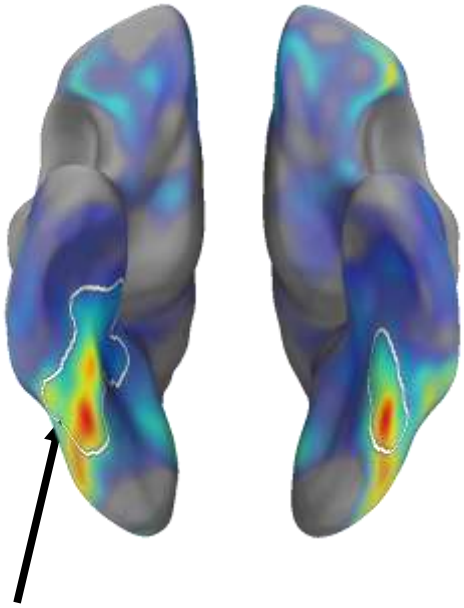
...reduced adaptation for faces

Typical Readers

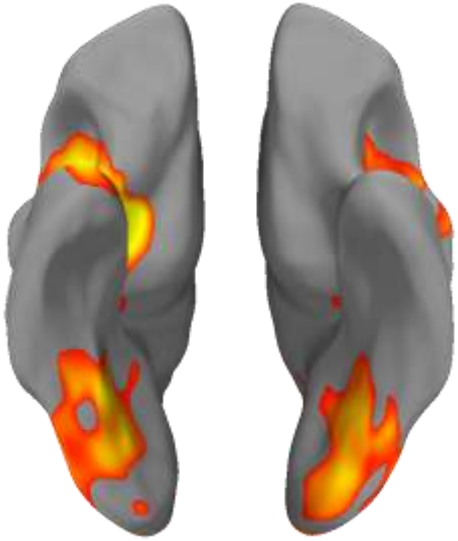


FFA

Dyslexia



FFA

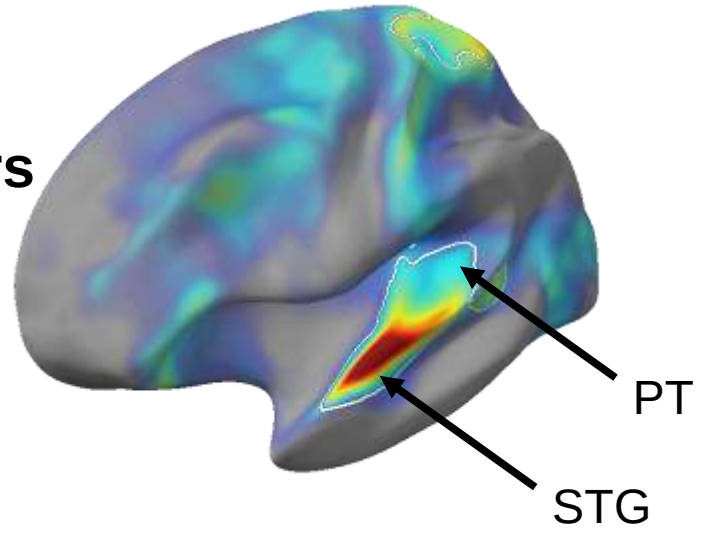


Group Difference

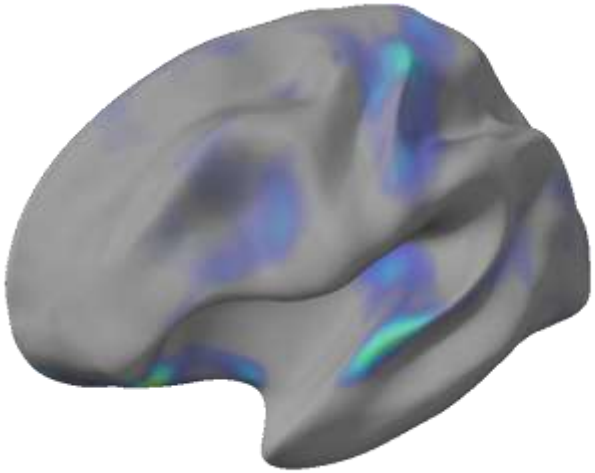
Perrachione *et al*. (2016) *Neuron*

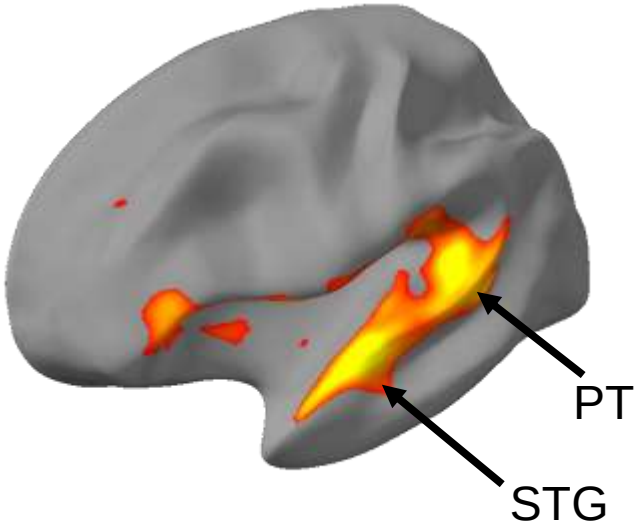
Reduced Adaptation in *Children* with dyslexia

Typical Readers



Dyslexia





Group Difference

Perrachione *et al*. (2016) *Neuron*

Brain Adaptation/Plasticity Difference in Dyslexia

Hypotheses

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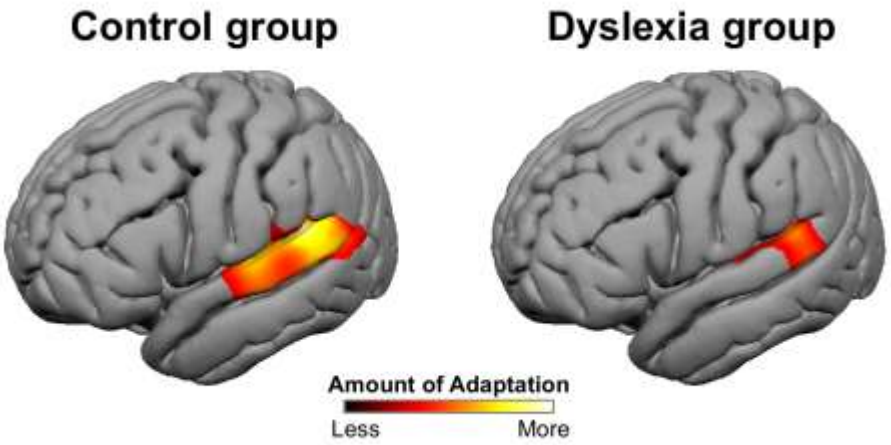
Reduced Adaptation/Plasticity in Dyslexia



- global in audition/vision (other senses?)
- present early in learning to read
- how a general difference in a brain mechanism can produce a specific difficulty in learning to read for brains because reading is based entirely on plasticity
- but why then is the difficulty so specific to reading?

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Can Neuroimaging Predict Future Reading Gains?

…better than reading, language, and other behavioral measures?

Predicting Compensation in Dyslexia

- **some children compensate, some children do not compensate**

what is the brain basis of compensation?

more like typical development?

an alternative brain pathway?

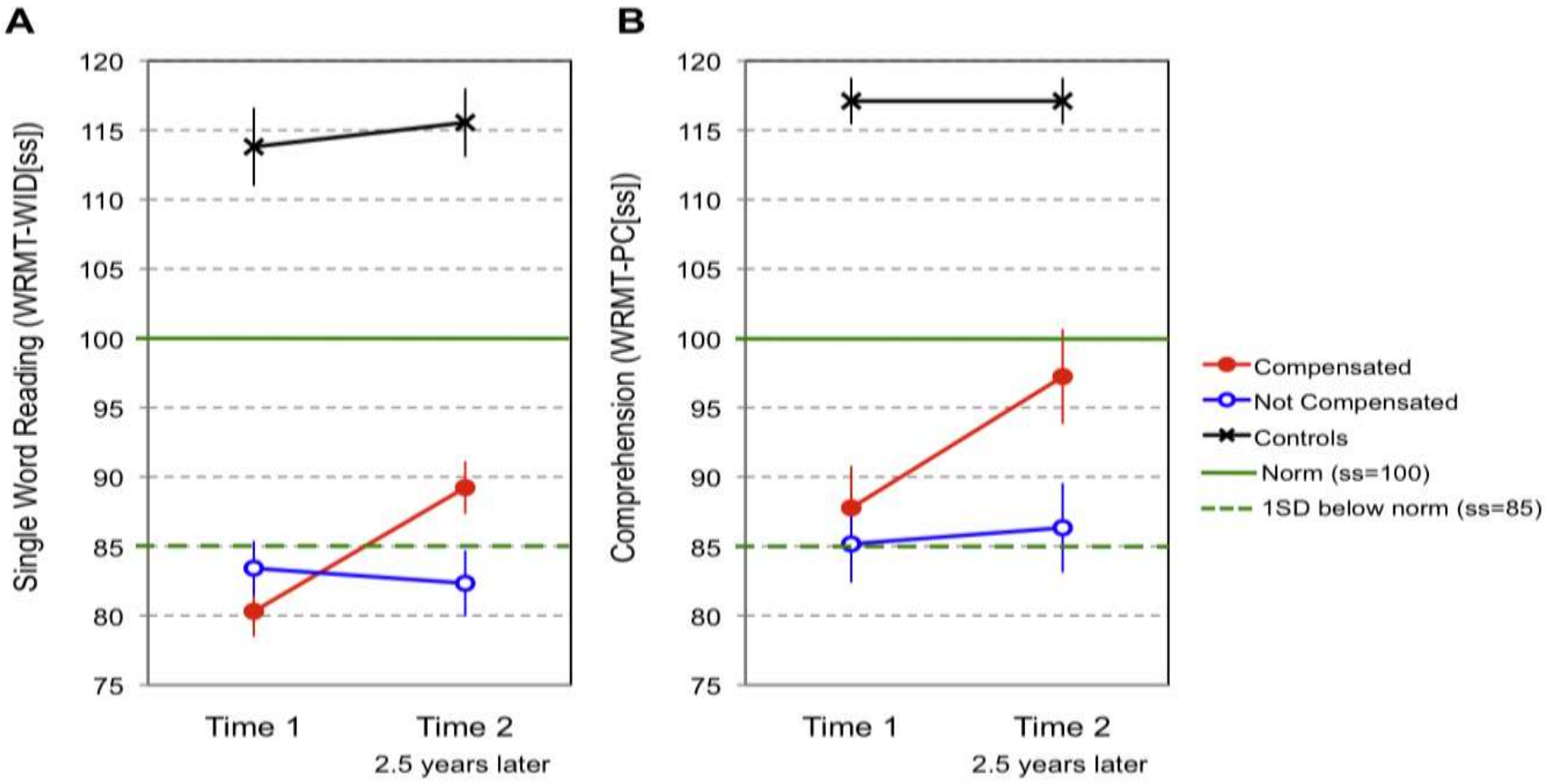
- **who compensates? who does not compensate?**

Predicting Compensation in Dyslexia

- **25 children with dyslexia, 20 typically reading children, ages 10-16**
- **Time 1 – fMRI on visual rhyme task of phonological ability, DTI, 17 behavioral measures (language, reading, IQ, others)**
- **2.5 years**
- **Time 2 – reading scores**

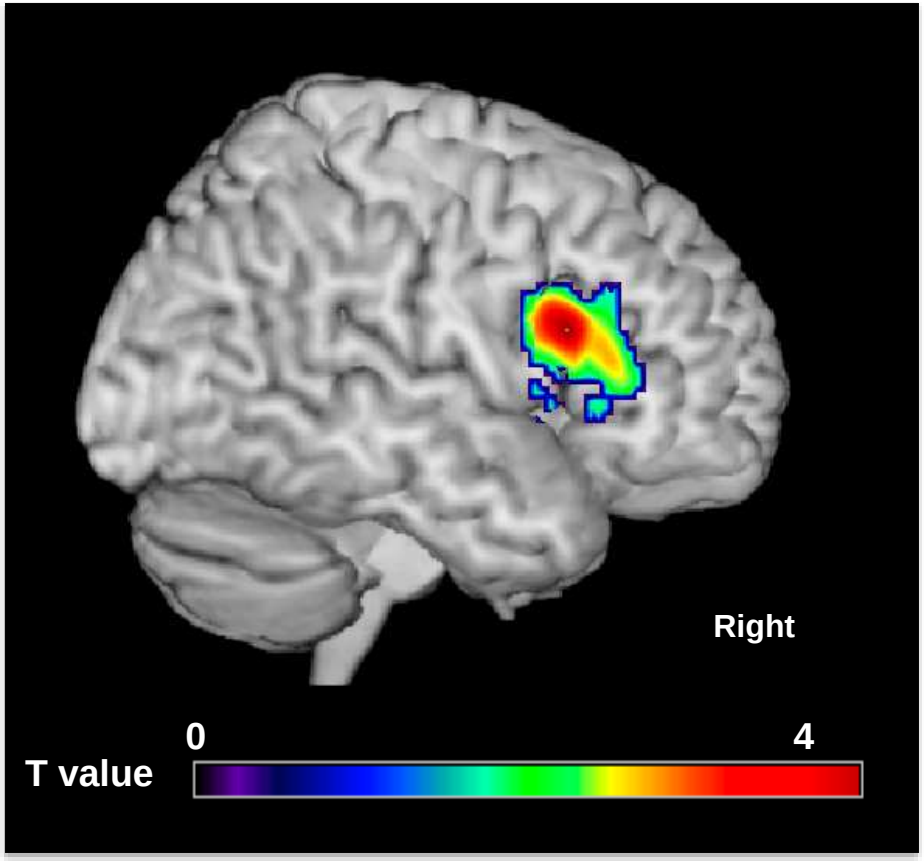
Hoeft et al., 2011, *PNAS*

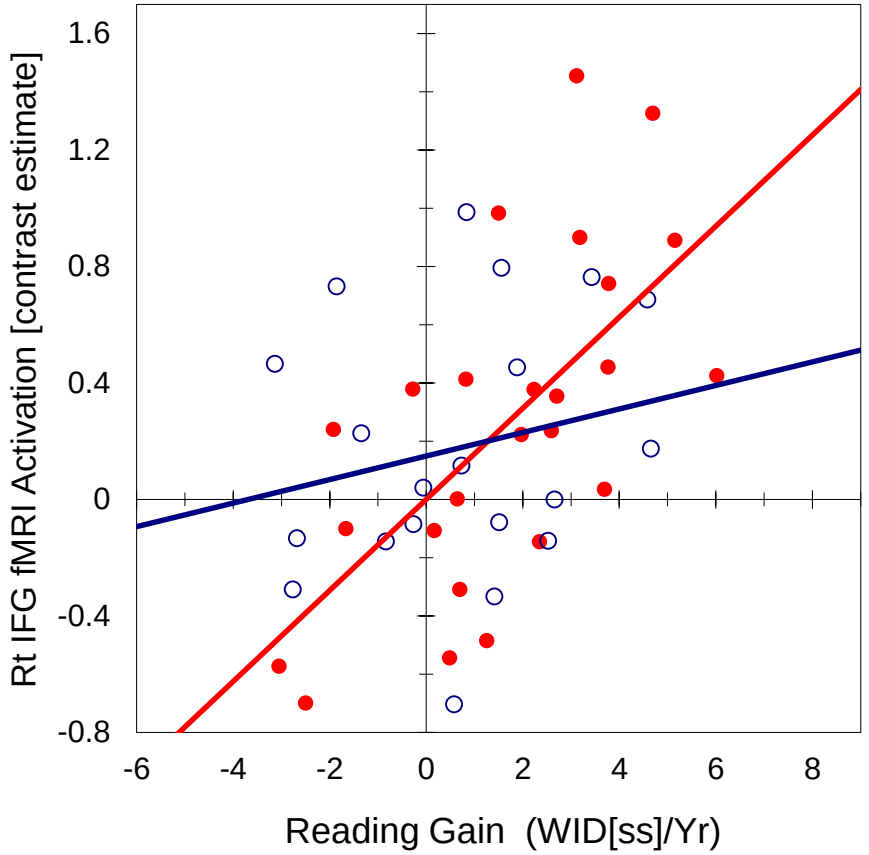
Compensation in Dyslexia Over 2.5 Years



Hoeft et al., 2011, *PNAS*

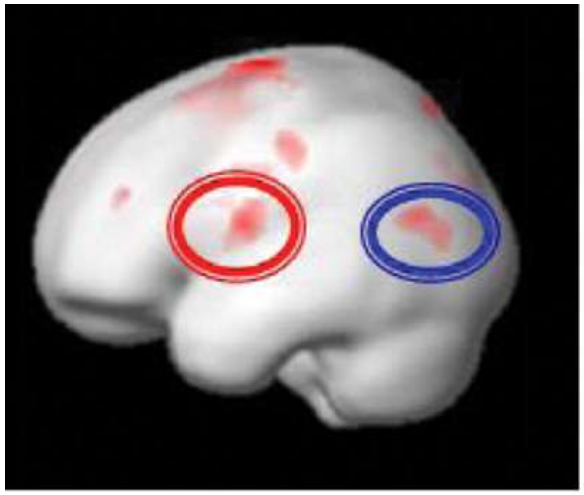
Activation in Right Frontal Cortex Predicts Compensation



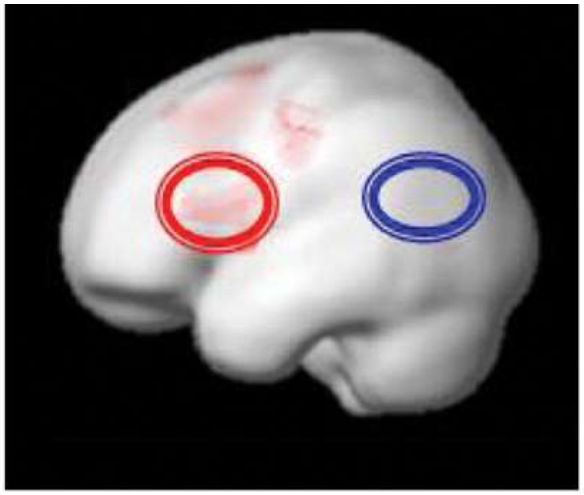


Hoeft et al., 2011, *PNAS*

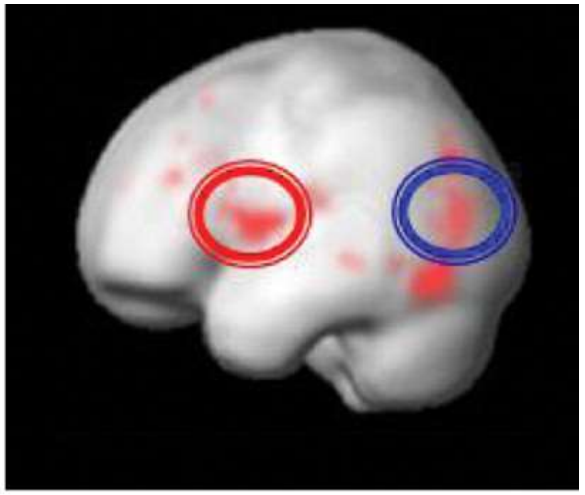
Brain Differences in Dyslexia & its Treatment



Typically reading children



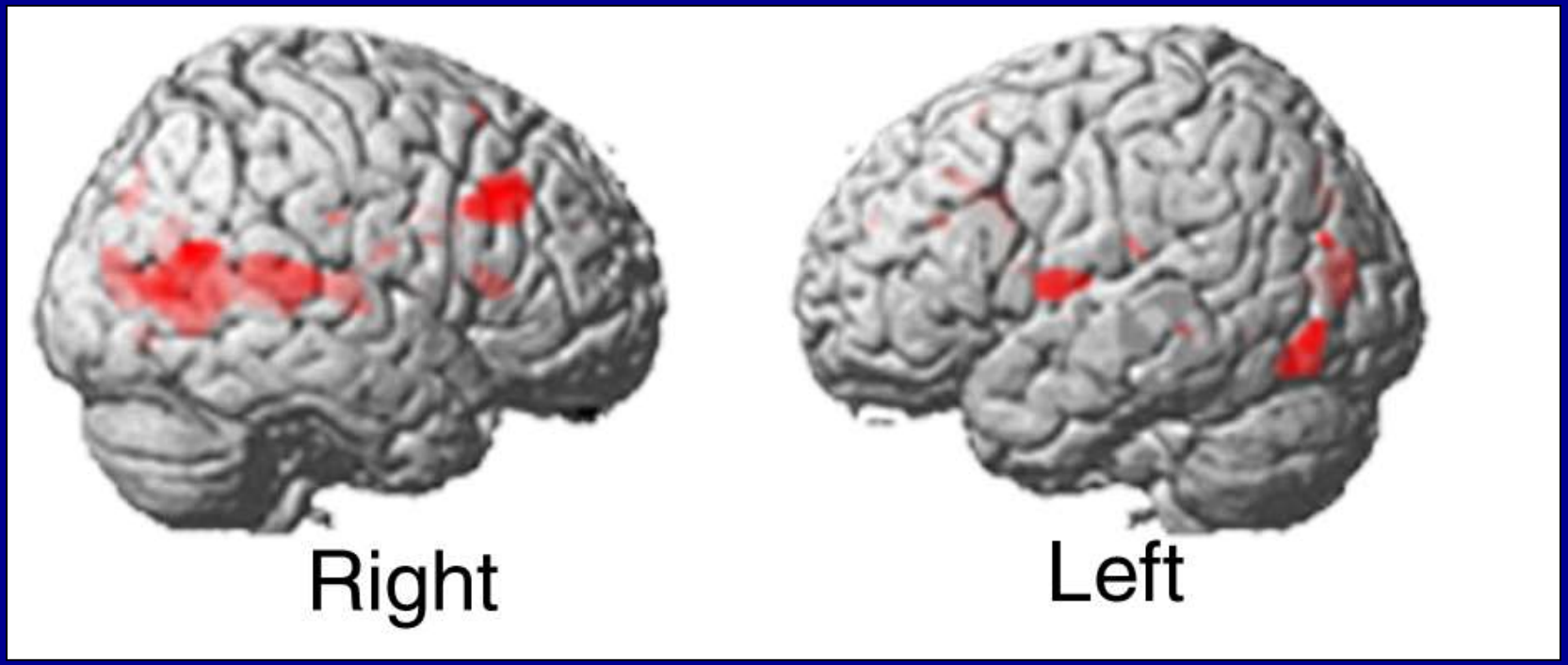
Children with dyslexia before remediation



Children with dyslexia after remediation

John D. E. Gabrieli Science 2009;325:280-283

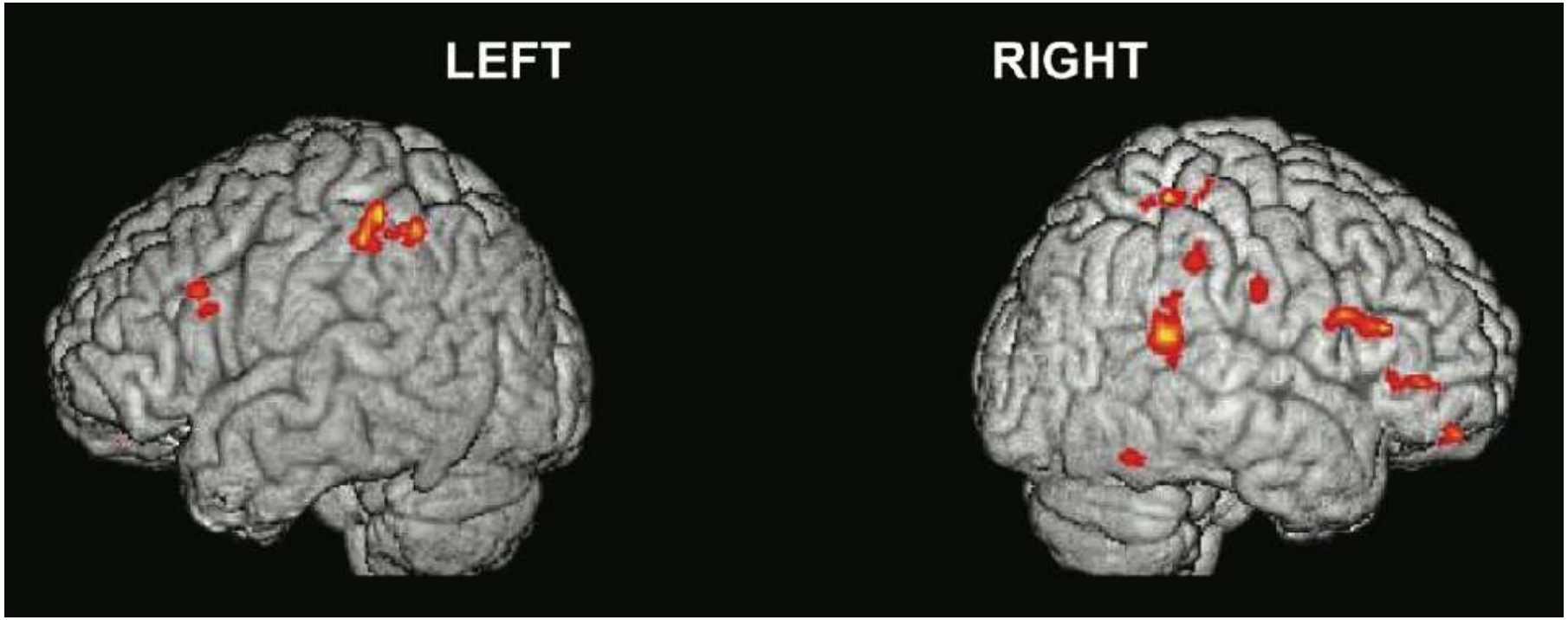
Brain Effects of Training: Phonological Processing



Compensation? ***Normalization?***

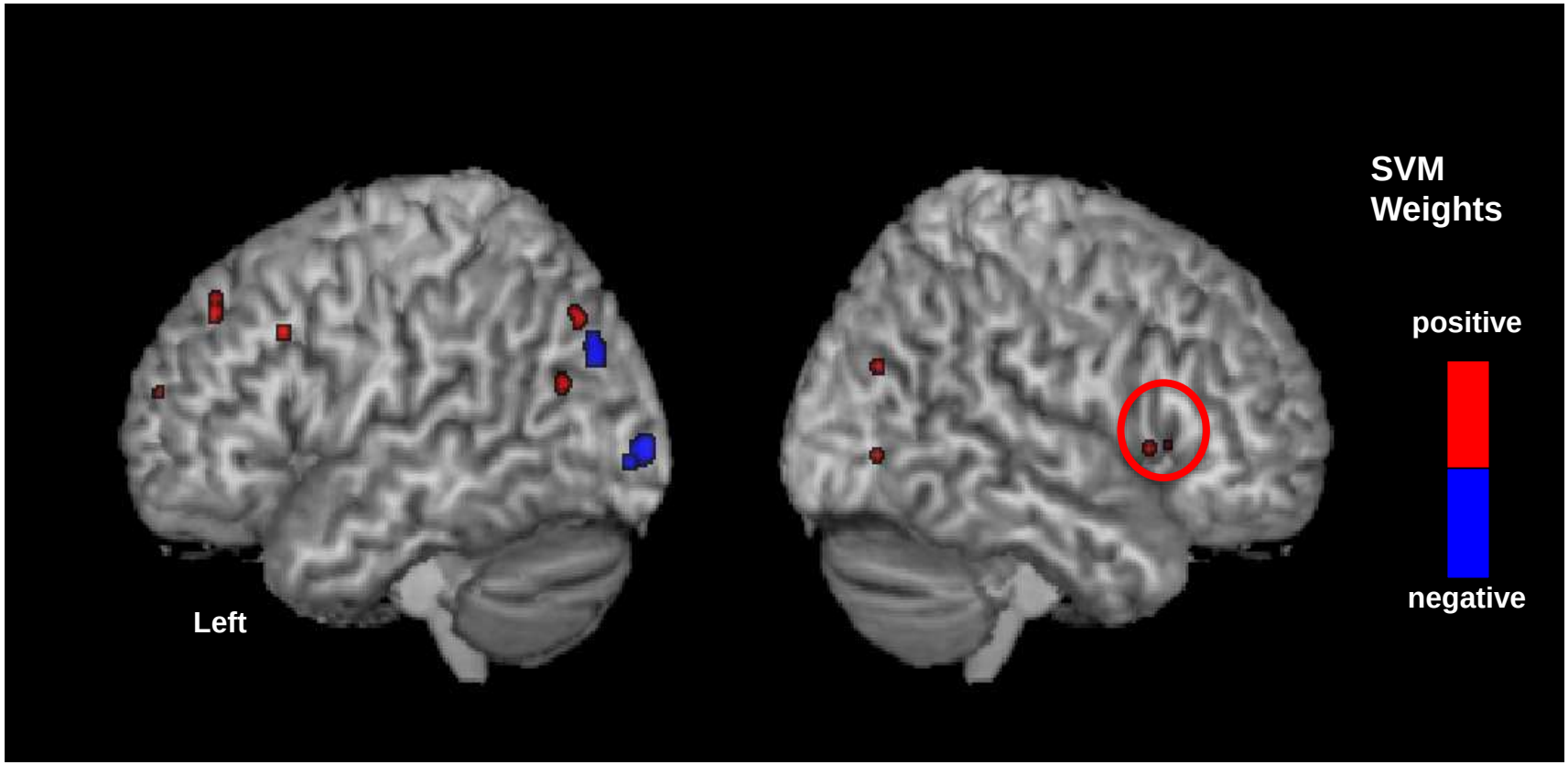
Brain Plasticity & Intervention

Increased Activation for Phonological Processing After Lindamood-Bell



Eden et al., *Neuron*, 2004

Multivoxel Pattern Analysis (Support Vector Machine)



Hoeft et al., 2011, *PNAS*

Predicting Compensation in Dyslexia

- **none of 17 behavioral measures predicts reading gains 2.5 years later, alone or in combination**
- **greater activation in right frontal cortex predicts compensation (66%)**
- **greater white matter integrity in right superior longitudinal fasciculus (52%)**
- **in combination, 72%**
- **multivoxel pattern analysis, 92%**

neuroprognosis?

Hoeft et al., 2011, *PNAS*

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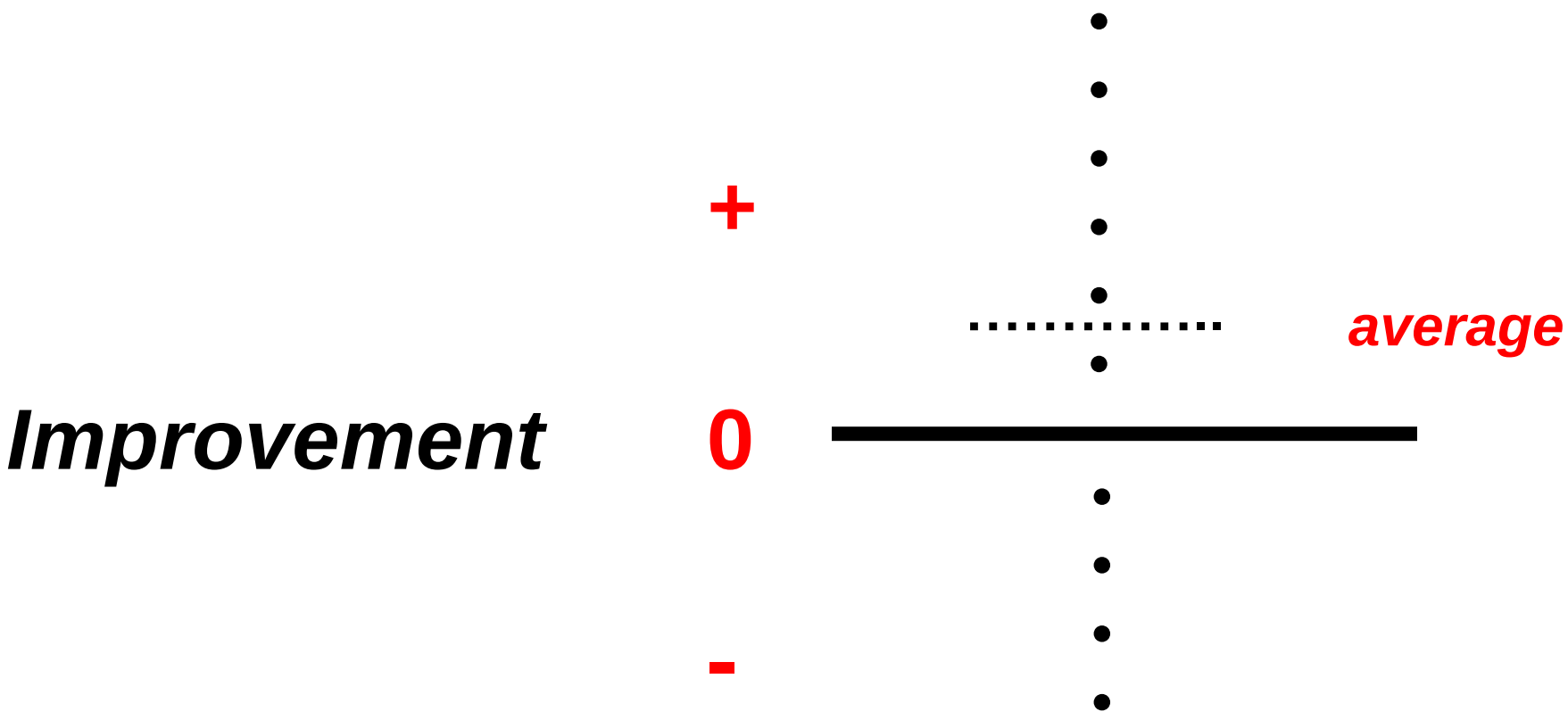
Interventions Work for Some Children, but not for all Children

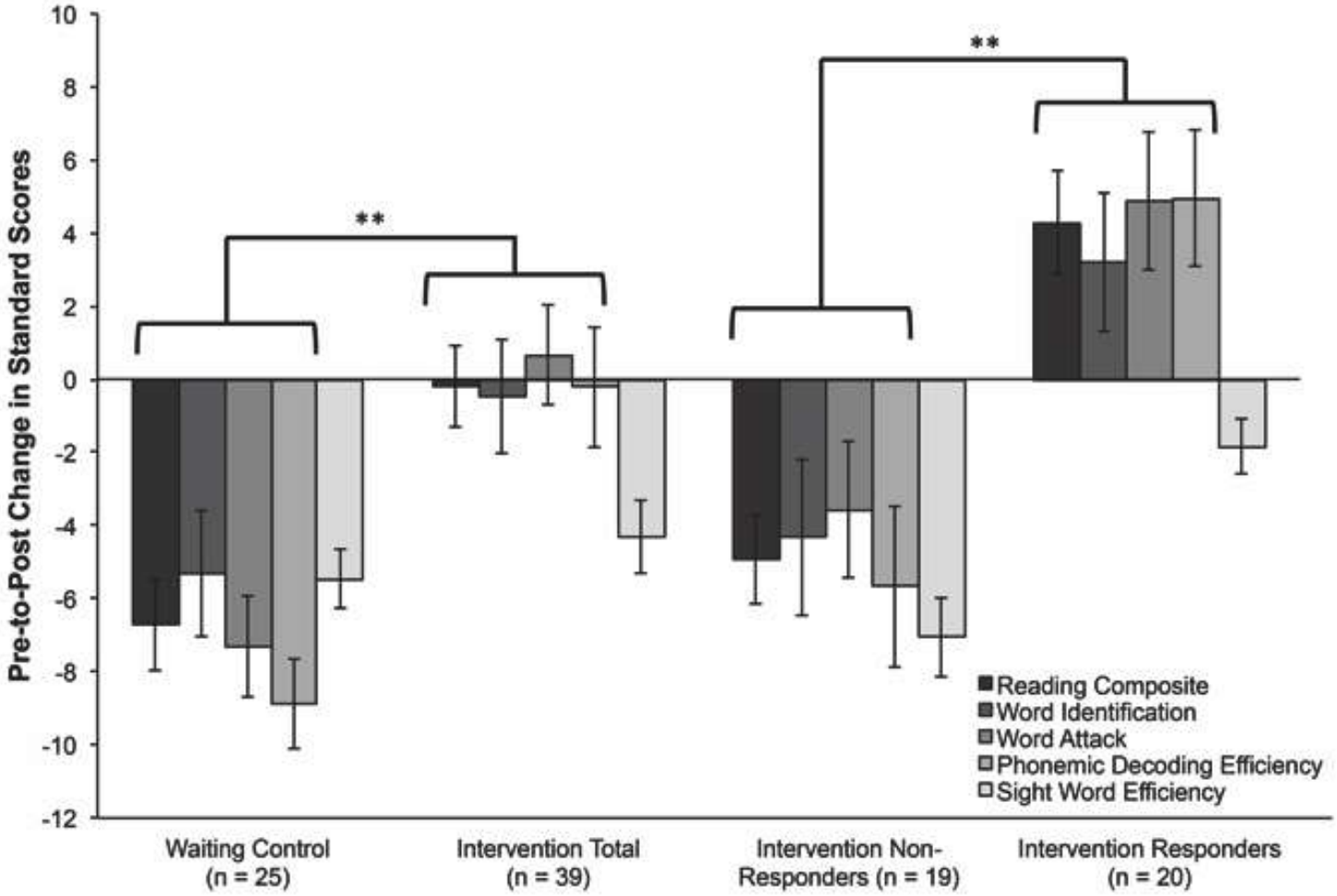


Summer Intervention with *See**ing Stars*** (Lindamood-Bell)

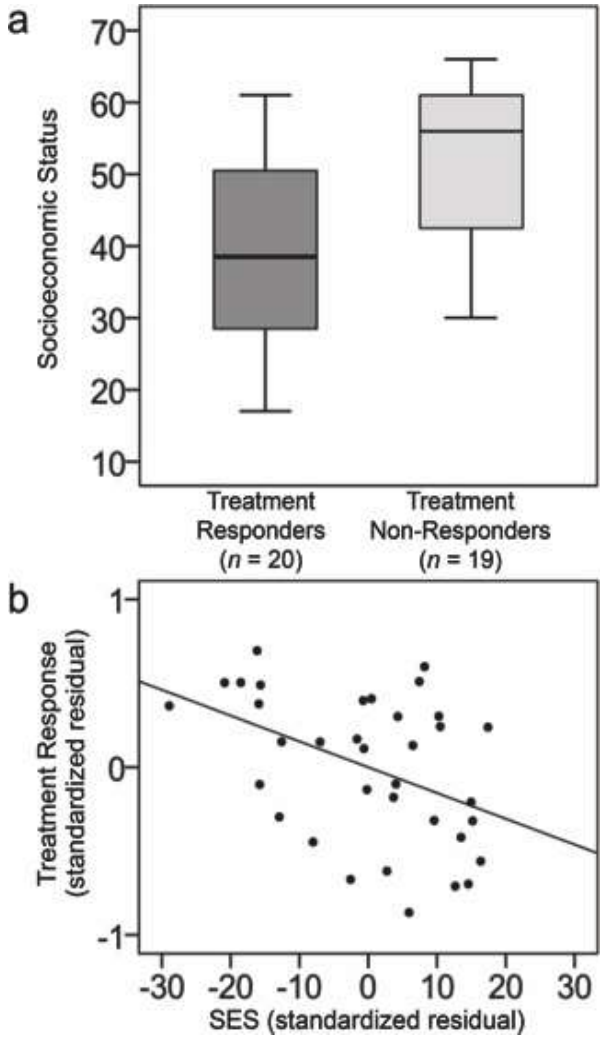
- **65 1st and 2nd graders with reading disability (RD)**
- **40 - 6 weeks/100 hours small group intervention**
- **25 - waiting-list controls**
- **diverse socioeconomic status (SES)**
  - **parental income, education, occupation**
- **structural brain imaging before and after**

Romeo et al., *Cerebral Cortex*,, *2017*

About Half of Children Responded to Intervention

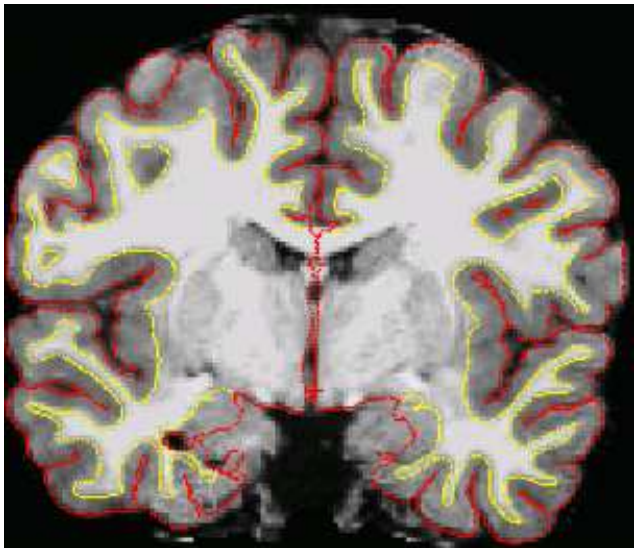


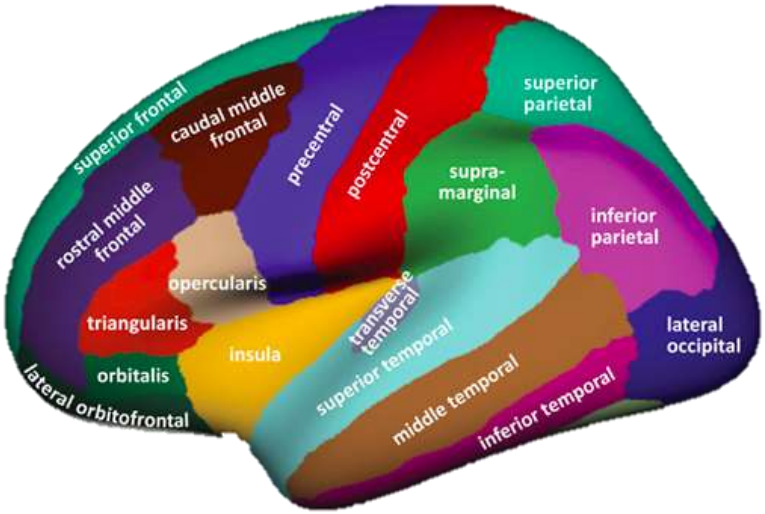
About Half of Children Responded to Intervention & Most of Those Were Lower SES

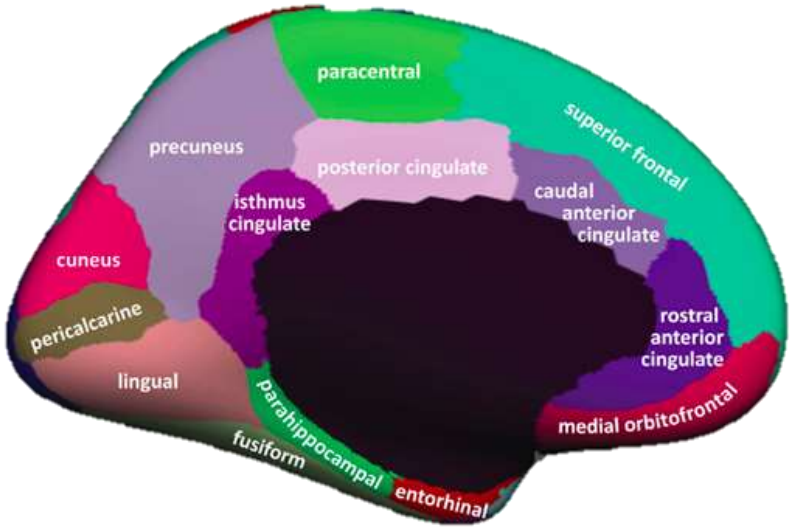


MRI – Lateral Views

Cortical Thickness Analysis





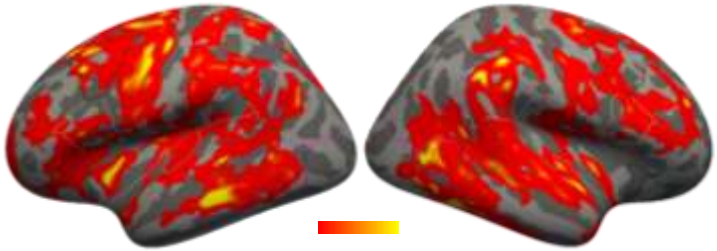


Only Effective Intervention Changes Brain Anatomy

No Intervention Control

Ineffective Intervention

Effective Intervention



Advances in Understanding Neuropsychological Bases of Dyslexia

- consistent brain differences in dyslexia
- brain differences in dyslexia present *before* learning to read in school

  early identification & prevention
- predicting improvement in dyslexia
- variation in response to intervention

  personalized learning – matching needs of each child with optimal support

Support: NSF & NIH