The Typical and Atypical Reading Brain

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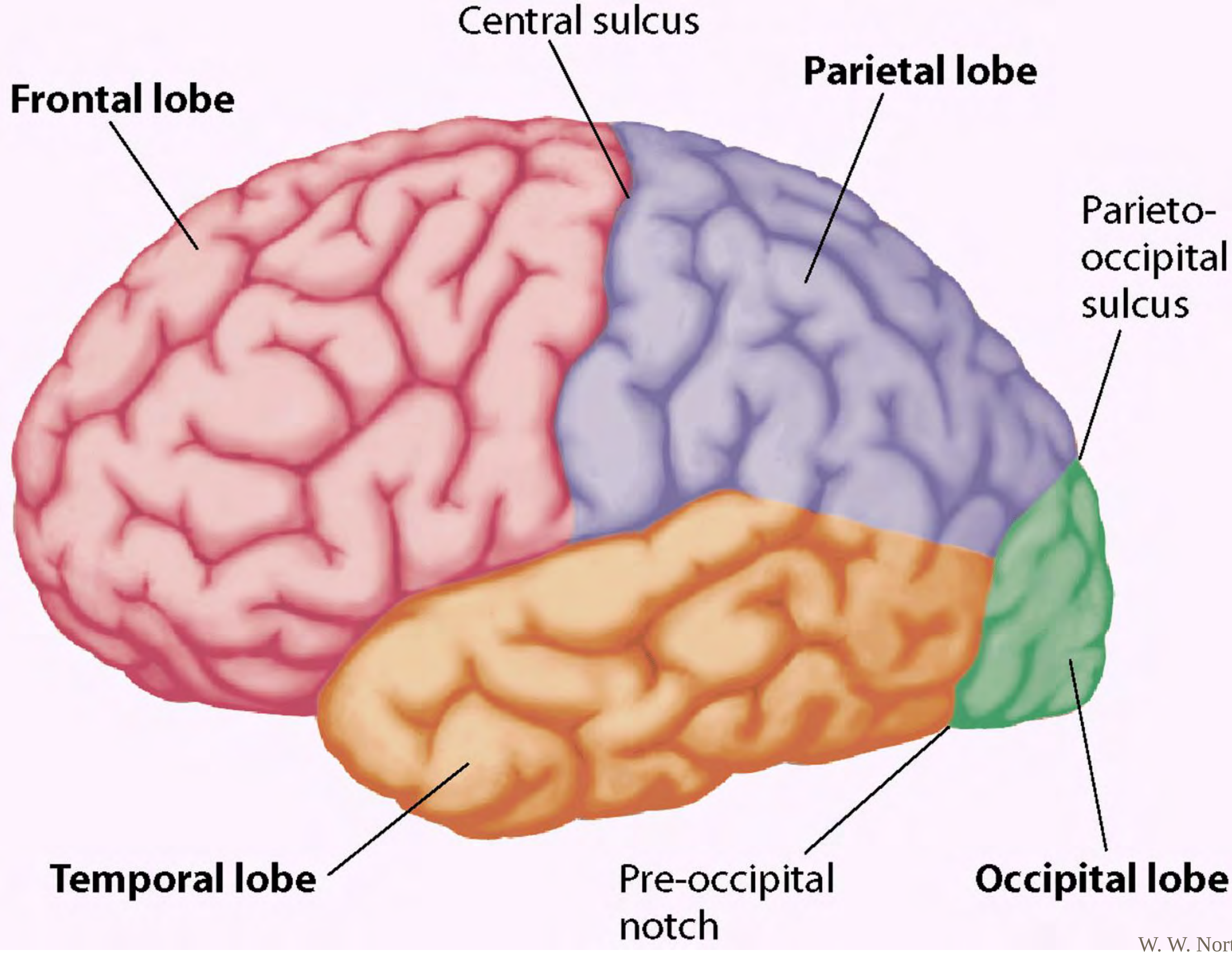
www.babymri.org

Overview

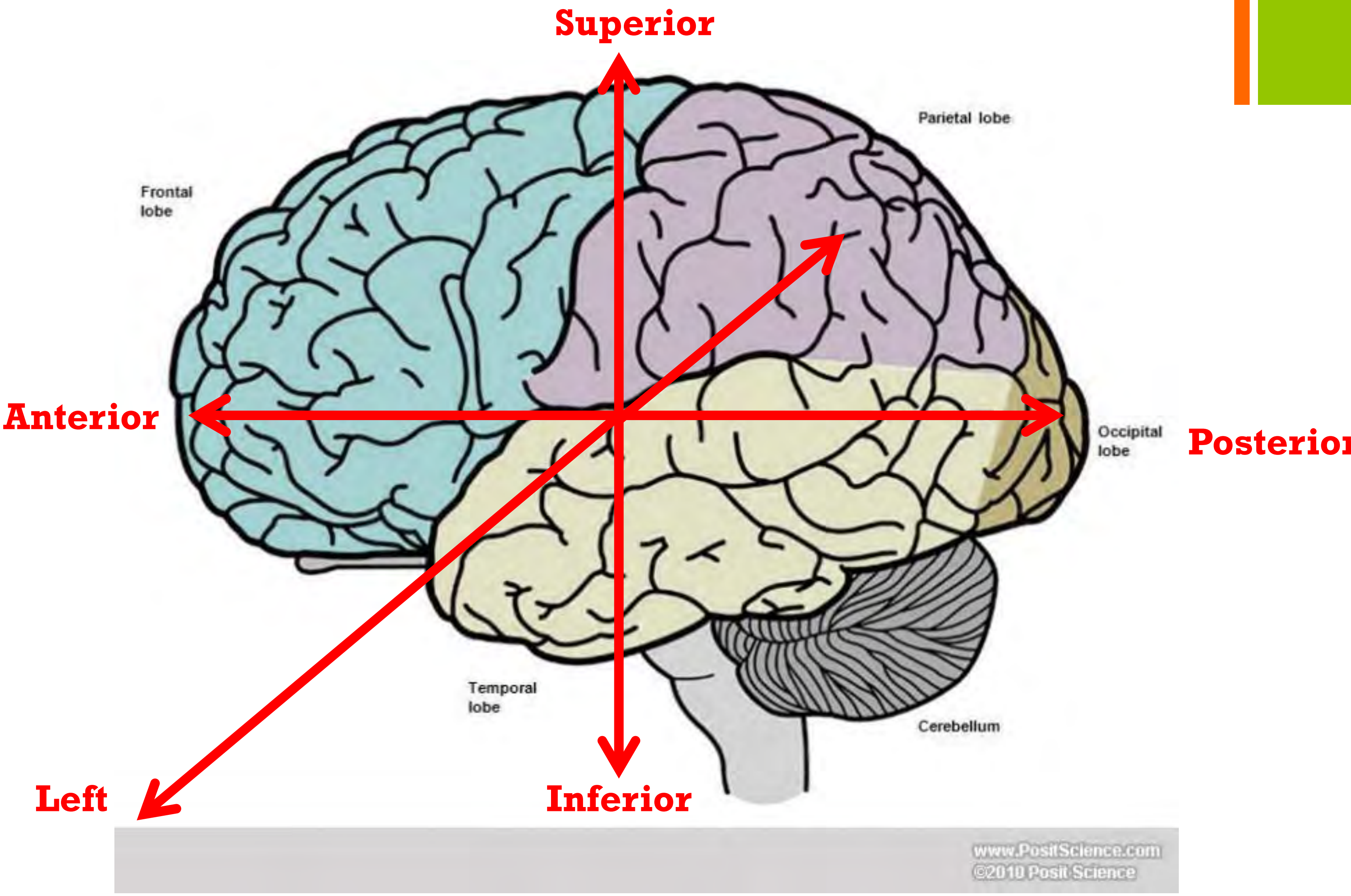
- Overview about the Brain
- The typical and atypical reading brain
- Remediating the reading brain
- Can brain measures enhance the accurate identification of children at risk for DD?
  - The Boston Longitudinal Dyslexia Study (BOLD).
  - Project READ (Research on the Early Attributes of Dyslexia)
- Detecting children at risk for DD in infancy?
- Educational and Clinical Implications



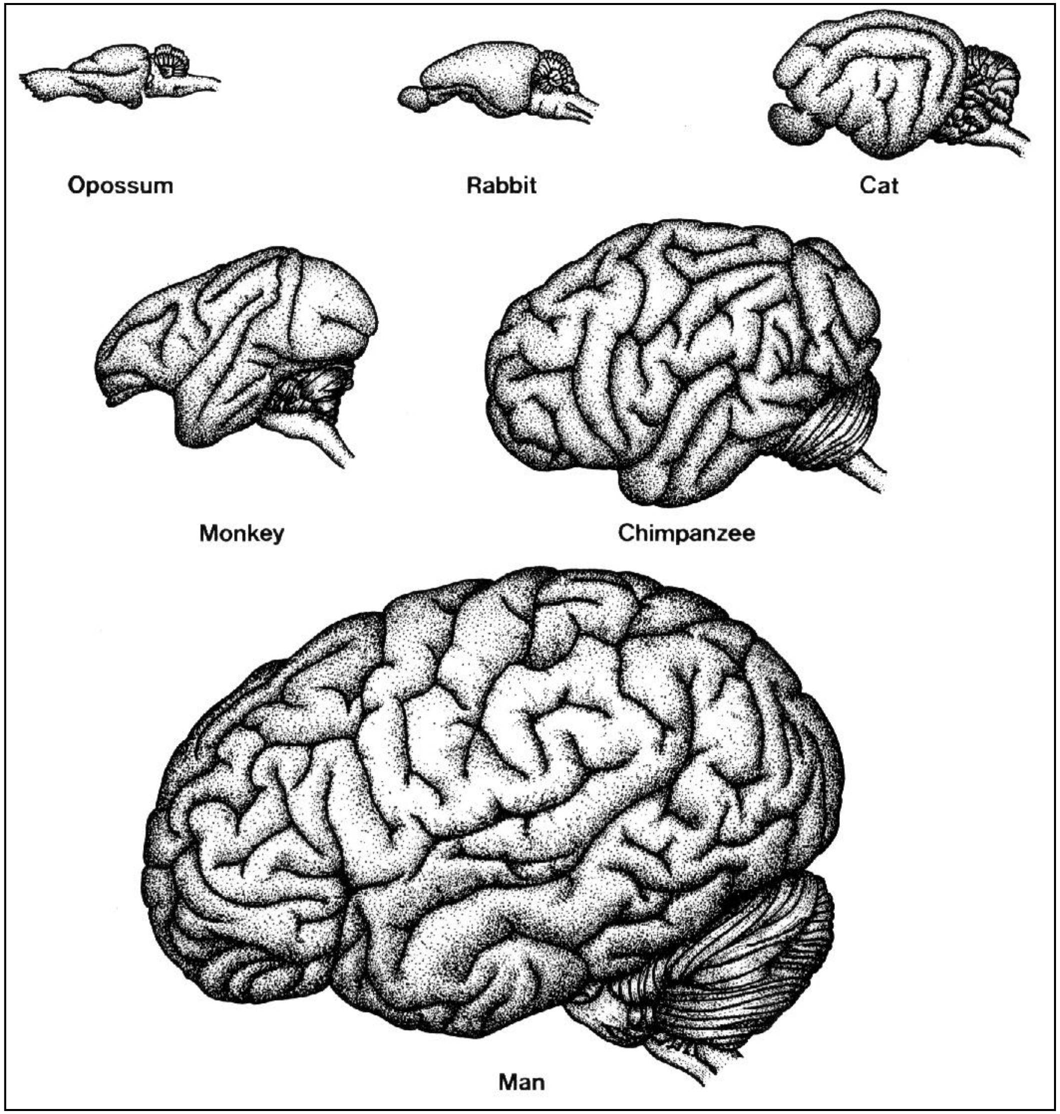
Central sulcus
Frontal lobe
Parietal lobe
Parieto-
occipital
sulcus
Temporal lobe
Pre-occipital
notch
Occipital lobe

W. W. Norton

Lobes & Directions



Brain Size: Is bigger better?



Atypical brain maturation

Sowell et al., 2006

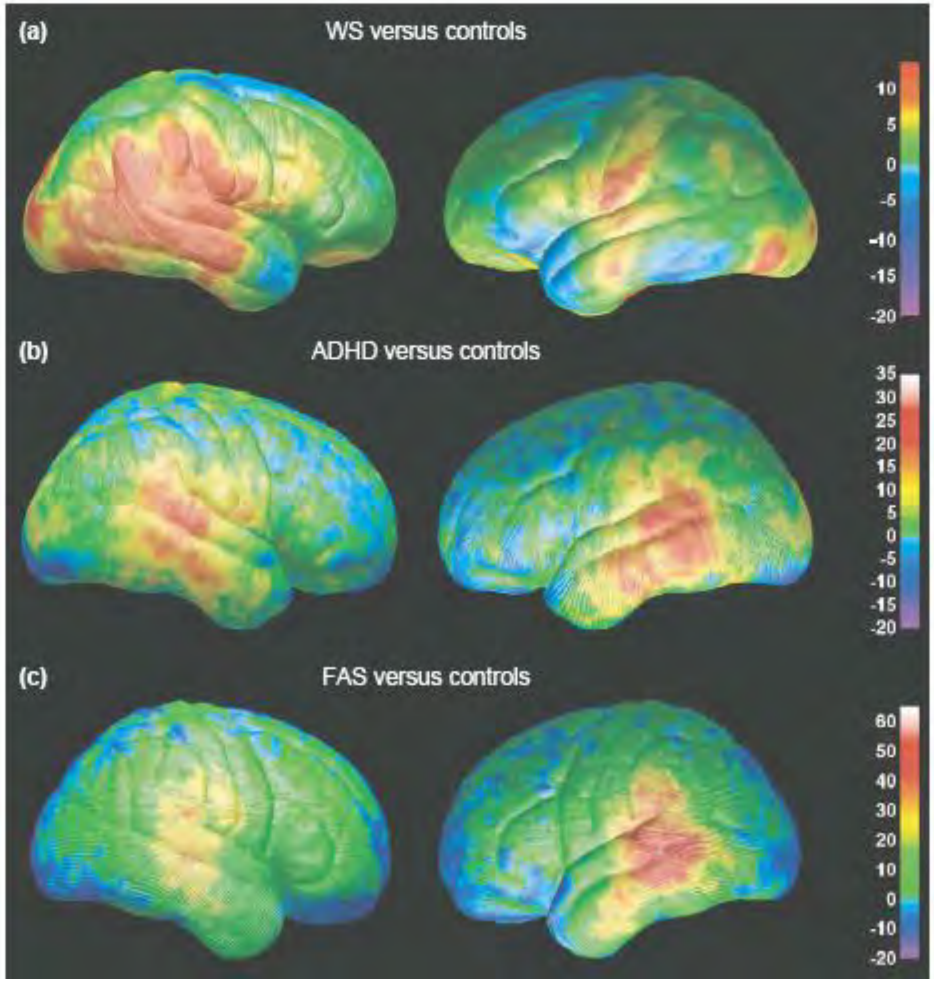
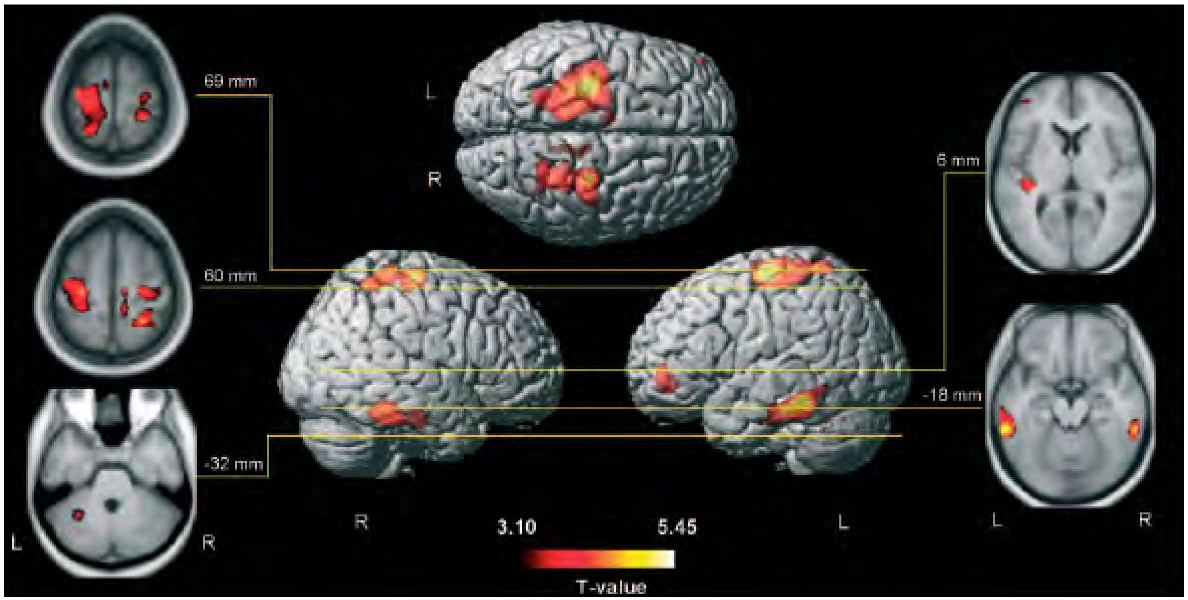


Figure 7. Differences in gray-matter density between subjects with three neurodevelopmental disorders. The percentage differences in gray-matter density between subjects with Williams syndrome (WS) (**a**), attention-deficit–hyperactivity disorder (ADHD) (**b**), fetal alcohol syndrome (FAS) (**c**) and their respective normally developing control groups are color-coded. In all maps, warmer colors represent positive differences, indicating an increase in the patient group (arbitrarily coded as 1) relative to the control group (arbitrarily coded as 0), with red representing the largest group difference. Note that the maximum value varies on the three color bars, depending on the maximum group difference from each comparison. Adapted, with permission, from [36,41,46].

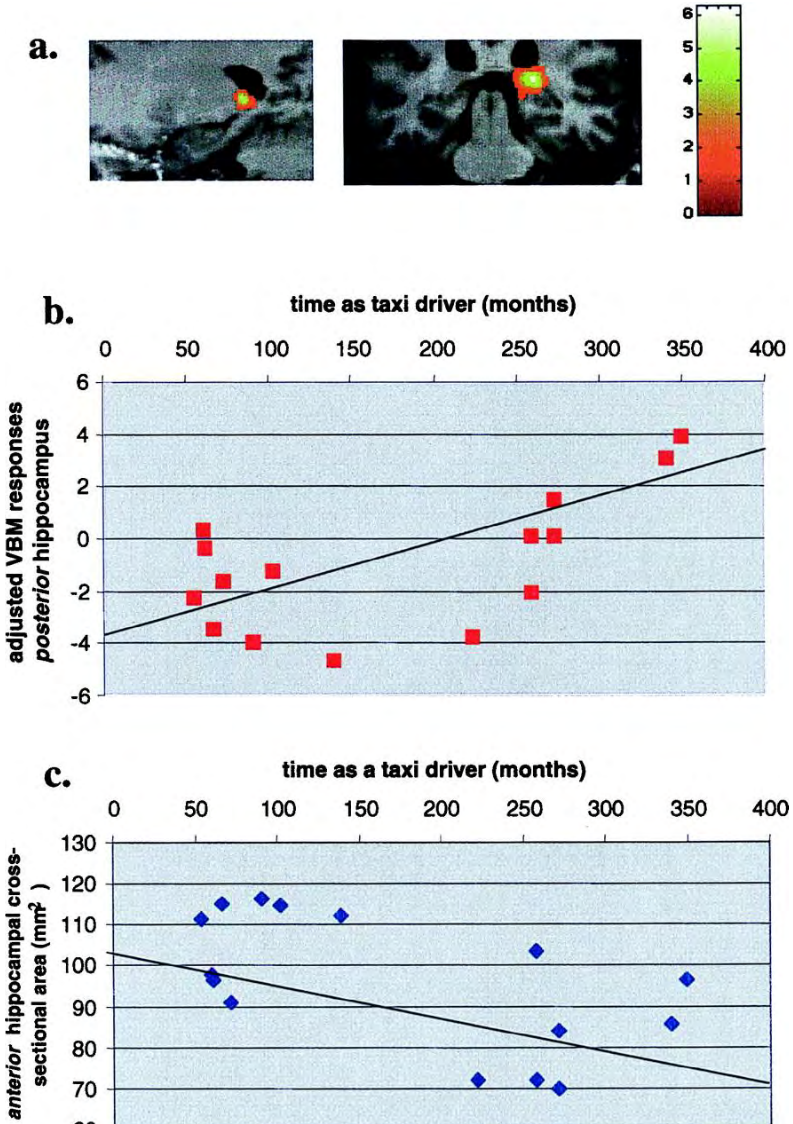
Anatomical differences between musicians and non-musicians



Brain regions with gray matter differences between professional musicians, amateur musicians and nonmusicians.

Gaser, Schlaug; 2003. The Journal of Neuroscience

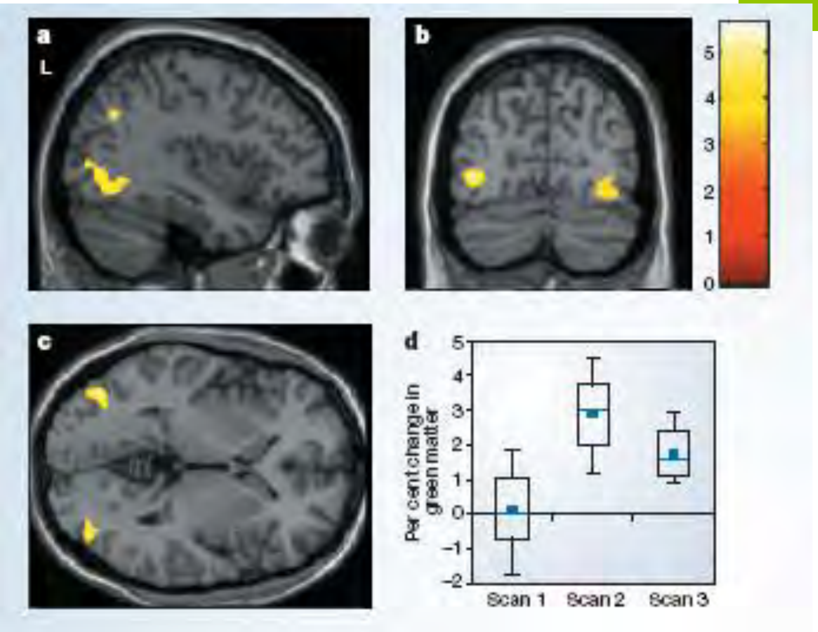
Plasticity in taxi drivers



Maguire et al., (2000)

Morphological changes induced by a short intervention

Draganski et al., 2004. Nature.



3 months training in juggling

Increased density of the grey matter in the jugglers compared to the non-juggler controls.

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What is Developmental Dyslexia?

- Affects 5-17% of children.
- Specific learning disability characterized by
  - difficulties with accurate and/or fluent word/text recognition.
  - poor spelling and poor decoding performance.
- Cannot be explained by poor vision or hearing, lack of motivation or educational opportunities.
- Familial occurrences as well as twin studies strongly support a genetic basis for DD.
- Currently up to seven theories that try to explain DD.
- No medications available.
- Strong psychological and clinical implications which start long before reading failure

Genetics

- Studies of families with DD suggest that DD is strongly heritable, occurring in up to 68% of identical twins and up to 50% of individuals who have a first degree relative with DD [Finucci *et al.,* 1984; Volger *et al.,* 1985).

- The genetic foundation of developmental disorders may be formed not by isolated genes, but rather by a combination of genes and the pathways that these genes regulate [Grigorenko, 2009].

- Several genes (e.g.; ROBO1, DCDC2, DYX1C1, KIAA0319) have been reported to be candidates for dyslexia susceptibility and it has been suggested that the majority of these genes plays a role in brain development. [e.g.; Galaburda *et al*., 2006; Hannula-Jouppi *et al*., 2005; Meng *et al.,* 2005; Paracchini *et al*., 2006; Skiba *et al*., 2011].

- It has been hypothesized that DD may be the result of abnormal migration and maturation of neurons during early development [e.g.; Galaburda *et al.,* 2006].

Psychological and Clinical Implications of DD

- Children with DD are often perceived by others as being ‘lazy’ or as those who ‘do not try enough.

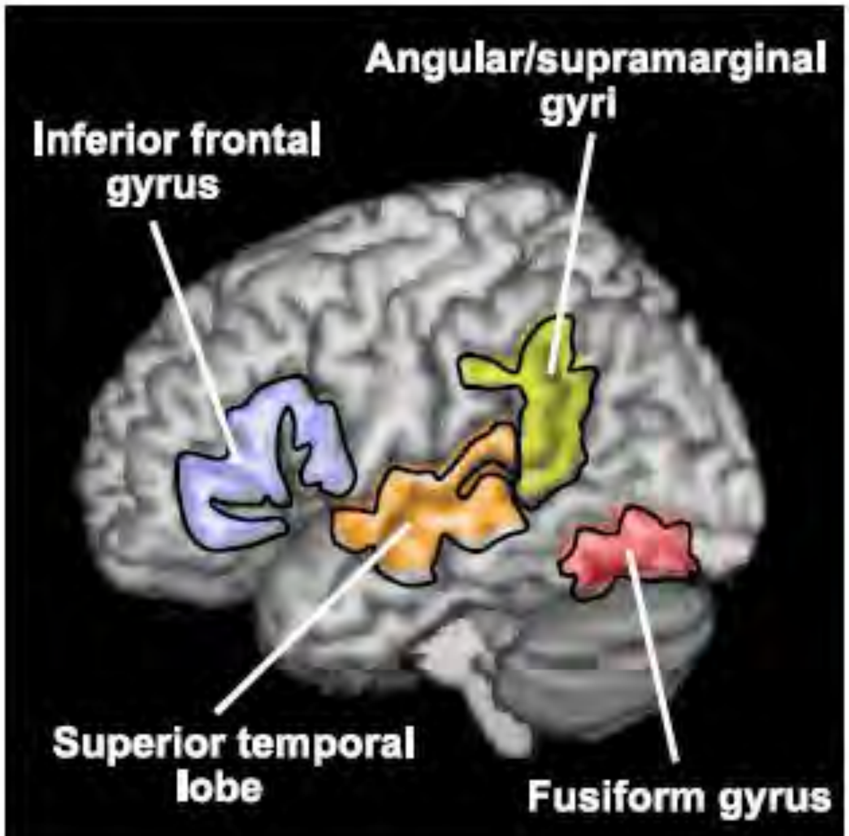
- Teachers, parents and peers often misinterpret the ‘dyslexic’ child’s struggle to learn as negative attitude or poor behavior and decreased self-esteem is often a result [Saracoglu *et al.,* 1989; Riddick *et al.,* 1999].

- These negative experiences leave children with DD vulnerable to feelings of shame failure, inadequacy, helplessness, depression and loneliness [e.g.; Valas *et al*., 1999].

- Possible anti-social behavior with long-standing consequences [Baker *et al.,* 2007].

- Less likely that these children will complete high school [Marder *et al.,* 1992] or join programs of higher education [Quinn *et al*., 2001], and increased probability that they will enter the juvenile justice system [Wagner *et al.,* 1993].

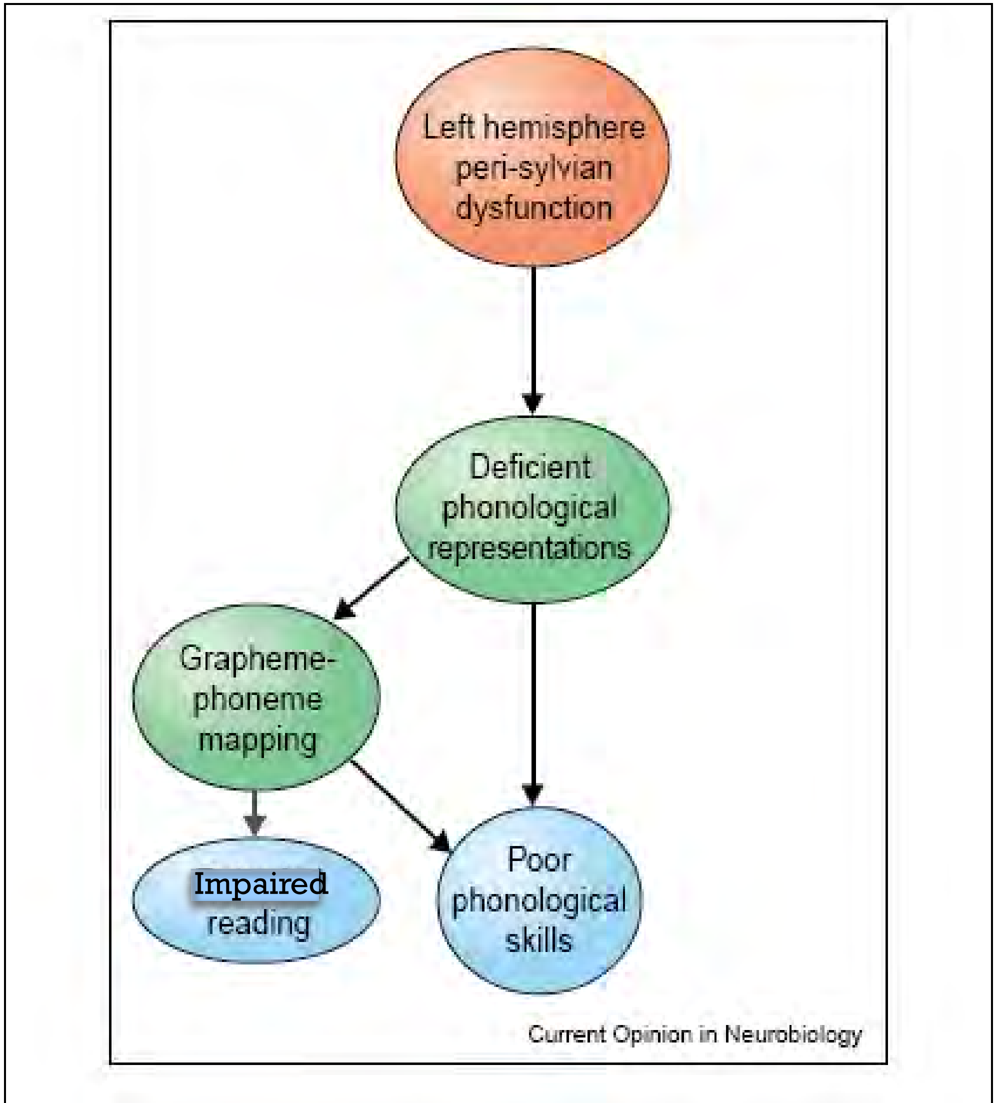
The typical reading network with its key components

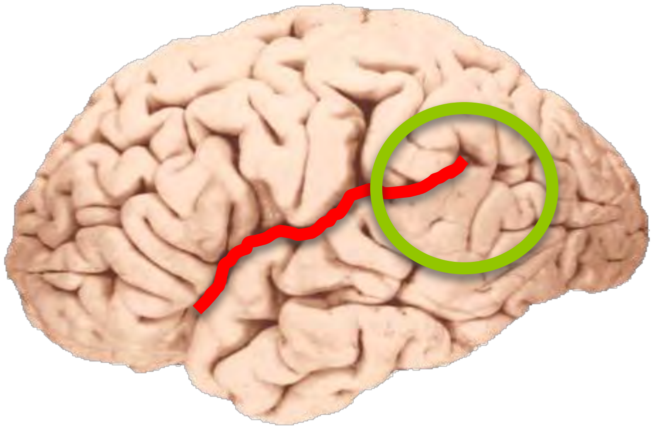


Mature reading is performed by a left hemispheric network. It maps visual (orthographical) information onto 'auditory' (phonological) and conceptual (semantic) representations.

Some of these functional areas seem to be fully developed in elementary school and some develop through adolescence [e.g.; Turkeltaub, *et al.*, 2003].

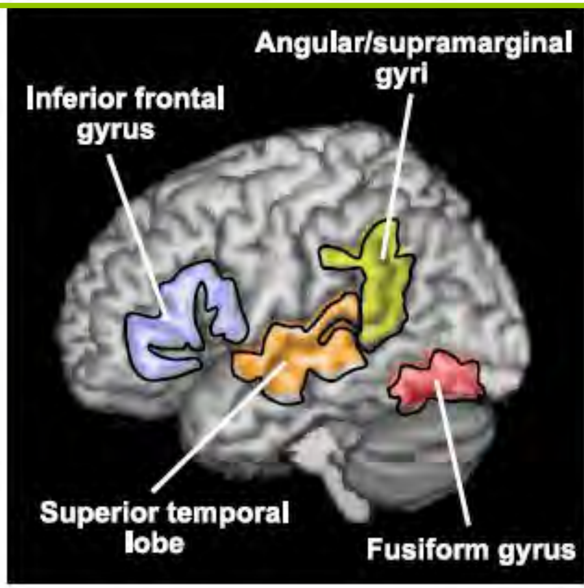
Several theories try to explain dyslexia:



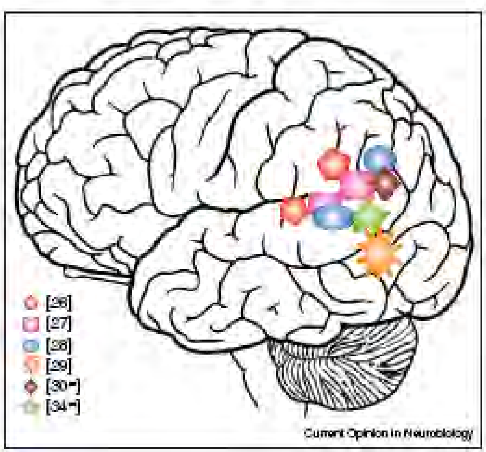


[after Ramus, 2003]

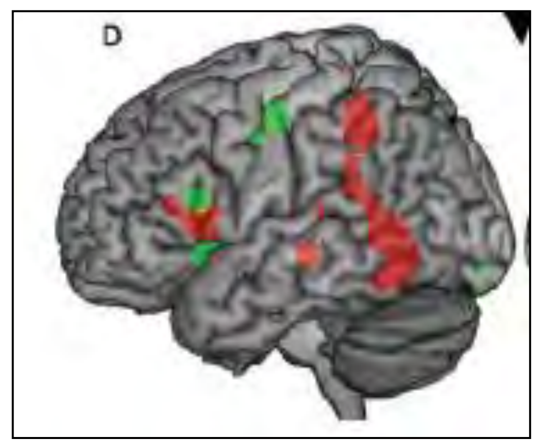
Typical reading network with its key components:



Temporo-parietal/Temporo-occipital dysfunction in dyslexia:

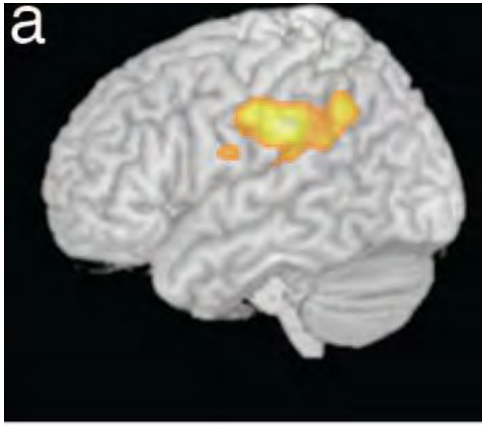


[Temple, 2002]

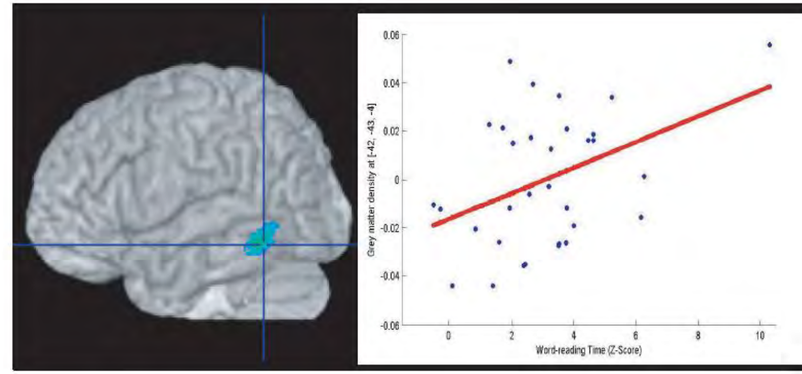


[Meta-analysis: 17 studies; Richlan *et al*., 2009]

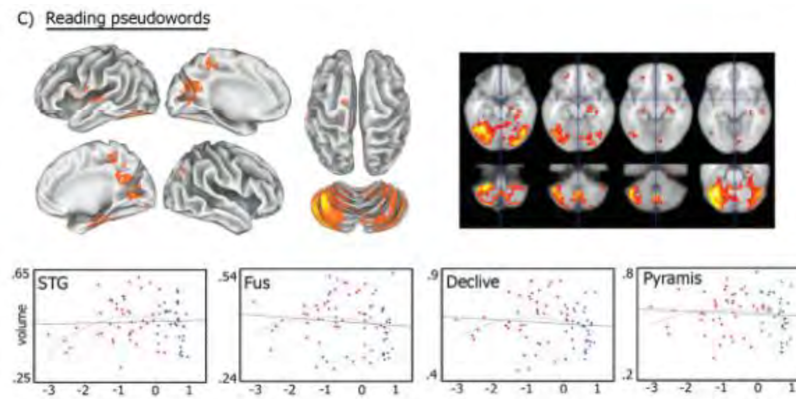
Structural brain differences (gray matter): Typical and atypical readers



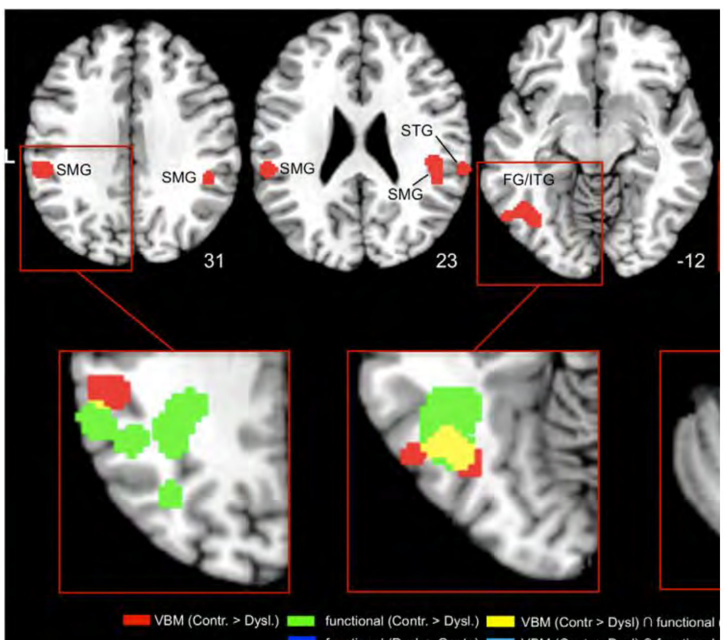
[Hoeft *et al.*, 2006]



[Silani *et al.*, 2005]



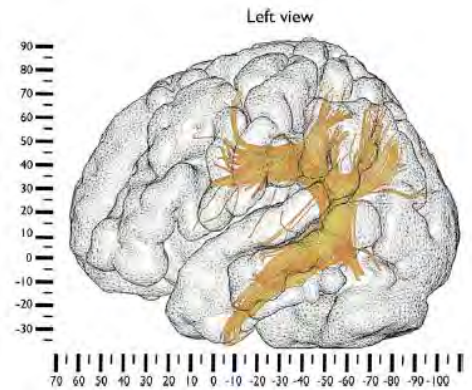
[Pernet *et al.*, 2009]



[Meta-analysis: Linkersdoerfer *et al.*, 2012]

[Steinbrink *et al.*, 2008]

Structural brain differences (white matter): Typical and atypical readers



[Catani, 2008]

- DD has been associated with structural differences in left-hemispheric white matter organization as measured by Diffusion tensor imaging tractography [e.g., Klingberg *et al*., 2000; Rimrodt *et al*., 2010; Steinbrink *et al.,* 2008].

- Most studies report alterations of the <u>Arcuate Fasciculus</u>, a neural pathway connecting the posterior part of the temporoparietal junction with the frontal cortex.

- Differences may reflect weakened white-matter connectivity among left-hemispheric areas that support reading. Measures (e.g.; fractional anisotropy) in left temporoparietal regions corelate positively with reading skills [e.g.,Deutsch *et al.,* 2005].

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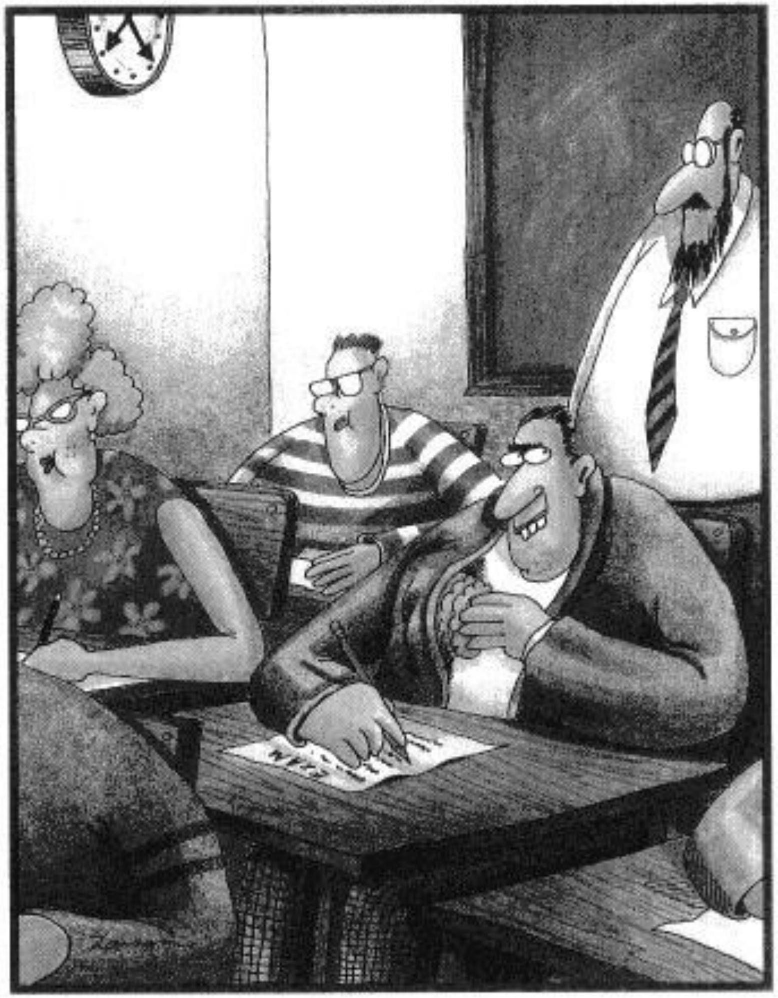
Brain Changes After Remediation



Midway through the exam, Allen pulls out a bigger brain.

Neural deficits in children with dyslexia ameliorated by behavioral remediation: Evidence from functional MRI

Elise Temple[†‡], Gayle K. Deutsch[§], Russell A. Poldrack[¶], Steven L. Miller[‖], Paula Tallal[‖††], Michael M. Merzenich[‖‡‡], and John D. E. Gabrieli[†§]

n= 45
Intervention:
Fast ForWord (8 weeks)

	Dyslexic-reading children				Normal-reading children			
	Pretraining	Posttraining	T-stat	P	1st scan	2nd scan	T-stat	P
Reading: WJ-RMT								
Word ID	78.2 (56–95)	86.0 (72–99)	3.9	0.0005	109.0 (95–120)	108.3 (97–126)	0.6	0.6
Word Attack	85.5 (72–102)	93.7 (82–109)	6.8	0.0001	112.3 (99–132)	109.4 (99–125)	1.1	0.3
Passage Comp	83.3 (51–103)	88.9 (77–107)	2.9	0.005	112.8 (104–120)	110.3 (100–122)	1.8	0.03
Language: CELF-3								
Receptive	92.5 (69–120)	101.3 (75–122)	3.6	0.001	118.6 (108–135)	121.8 (108–139)	1.5	0.2
Expressive	95.0 (61–125)	102.2 (80–150)	2.8	0.006	112.3 (102–125)	113.8 (92–139)	0.5	0.6
Rapid Naming	79.1 (35–97)	86.5 (67–103)	2.8	0.006	106.8 (94–121)	104.3 (82–124)	0.9	0.4

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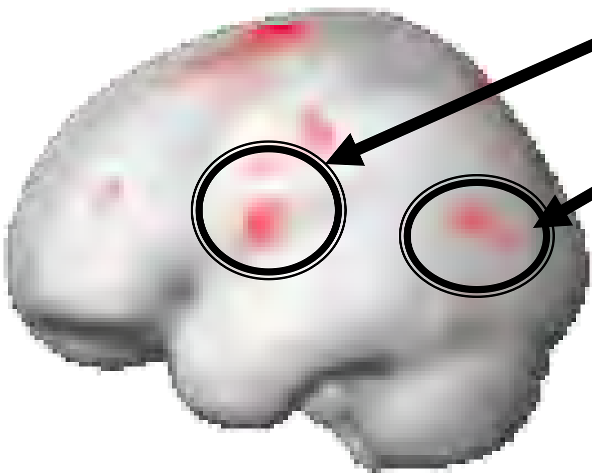
n= 45
8 weeks intervention

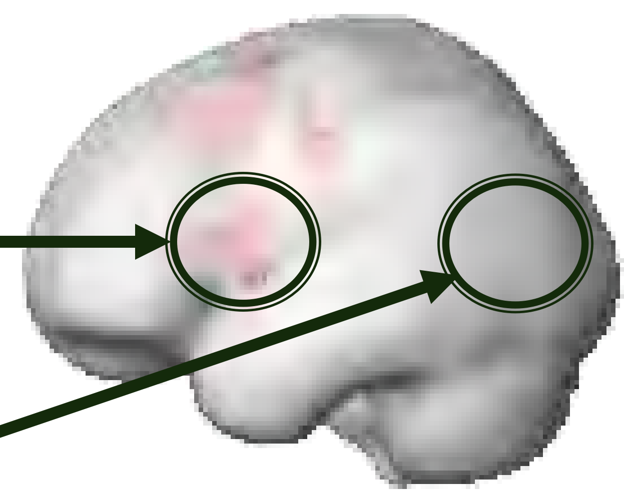
Control



Frontal AND Temporo-parietal

Dyslexia

Frontal but NOT Temporo-parietal

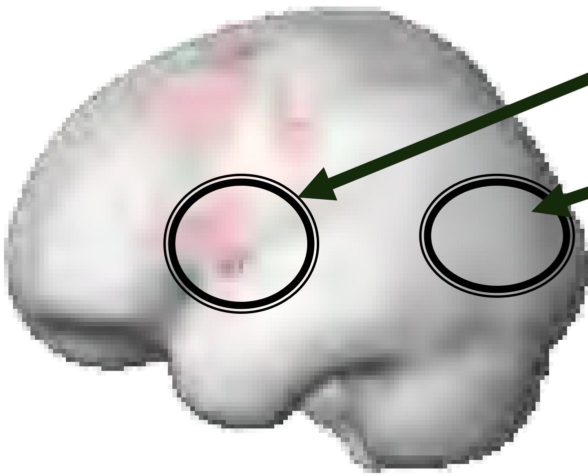


Example:
B D = Rhyme
B K = Do Not Rhyme

[Temple et al. (2003) PNAS, 100]

Neural effect of intervention

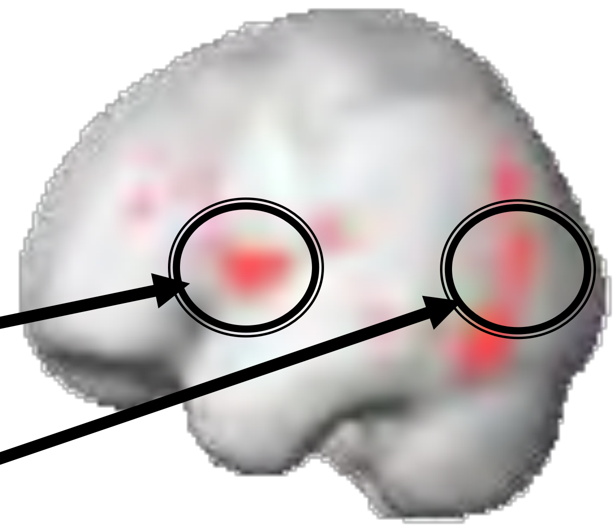
Pre-Intervention



Frontal but NOT Temporo-parietal

Post-Intervention

Increased activity in Frontal AND Temporo-parietal



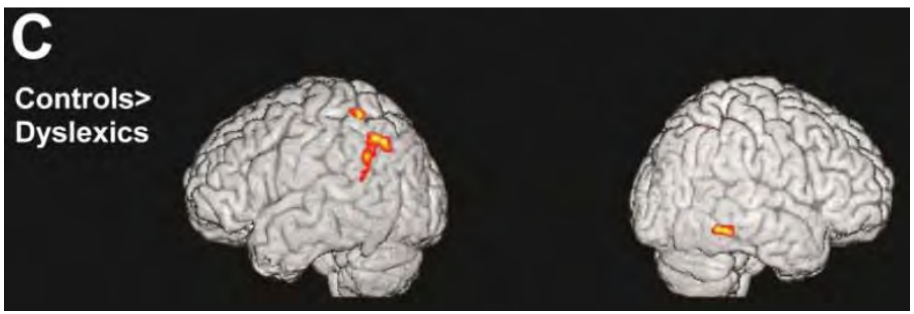
After training, metabolic brain activity in dyslexics more closely resembles that of typical readers.

[Temple et al. (2003) PNAS, 100]

Neural Changes following Remediation in Adult Developmental Dyslexia

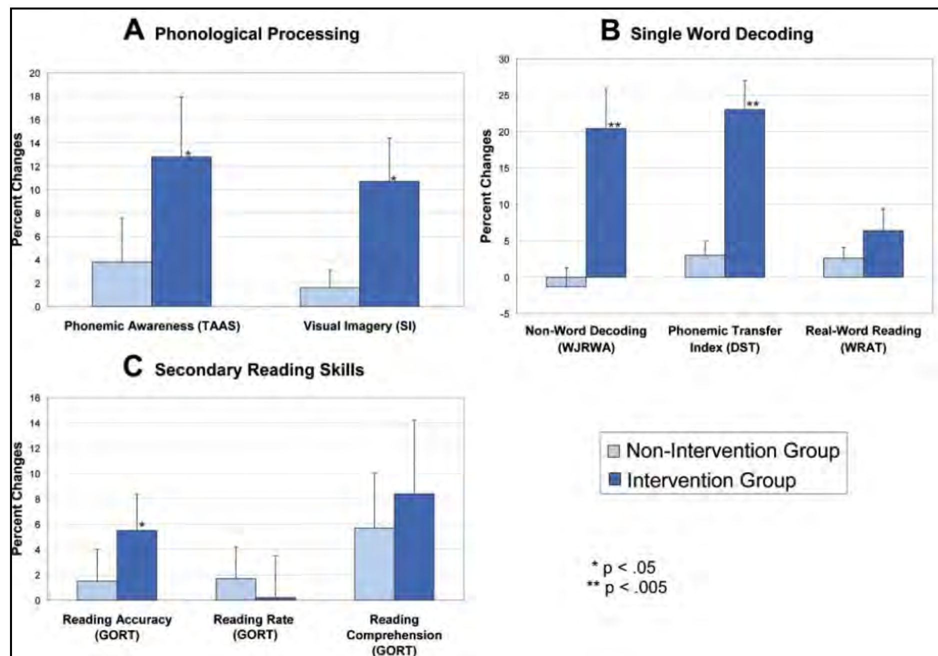
Guinevere F. Eden,[1,*] Karen M. Jones,[1] Katherine Cappell,[1] Lynn Gareau,[1] Frank B. Wood,[2] Thomas A. Zeffiro,[1] Nicole A.E. Dietz,[1] John A. Agnew,[1] and D. Lynn Flowers[1,2]

n= 38
Intervention: Lindamood-Bell (8 weeks)



Sound deletion > word repetition

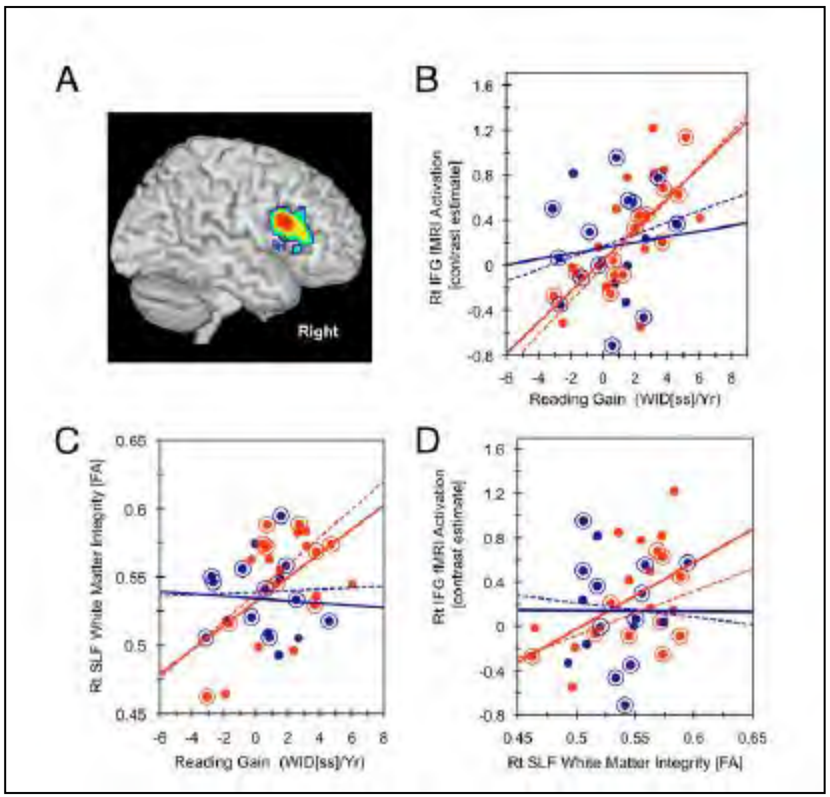
Post remediation > Pre-remediation



Neural systems predicting long-term outcome in dyslexia

Fumiko Hoeft[a,b,1], Bruce D. McCandliss[c], Jessica M. Black[a,d], Alexander Gantman[a], Nahal Zakerani[a], Charles Hulme[e], Heikki Lyytinen[f], Susan Whitfield-Gabrieli[g], Gary H. Glover[h], Allan L. Reiss[a,b,h], and John D. E. Gabrieli[h]

- Who compensates? Brain measures predicted with 92% accuracy which individual children improved and which individual children did not improve 2.5 years later (Hoeft et al., 2011)



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The ‘Dyslexia Paradox’

- To date, the earliest that DD can be reliably diagnosed is in second/third grade and most children exhibit enduring reading impairments throughout adolescence and into adulthood [e.g.; Francis & Shaywitz, 1996; Juel *et al*., 1988; Torgesen & Buress, 1998].

- Intervention studies are most effective in kindergarten and first grade. When “at risk” beginning readers receive intensive instruction, 56% to 92% of at-risk children across six studies reached the range of average reading ability [Vellutino *et al.,* 2004].

The Boston Longitudinal Dyslexia Study (BOLD)

Early Identification children at-risk

Diagnosis Dyslexia

Preschool Kindergarten 3rd grade Middle School

- Functional MRI
- Structural MRI
-Behavioral tests
-Psychophysics
-Questionaires
-DNA

Follow up:
-prior to first grade
-prior to second grade
-prior to third grade

- To date 114 children enrolled longitudinally (64 FHD+/50 FHD-).
- Pre-readers (Word ID <5), reading instruction within next year.

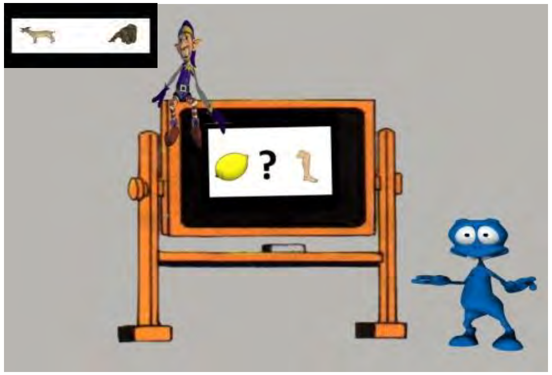
Psychometric Measures:
- Clinical Evaluation Language Fundamentals –Preschool 2
- Comprehensive Test Of Phonological Processing
- Grammar And Phonology Screening Test
- York Assessment for Reading for Comprehension
- Rapid Automatized Naming and Rapid Alternating Stimulus Test
- Kaufman Brief Intelligence Test 2
- Year 2: Word reading (timed/untimed), passage comprehension, fluency, spelling, letter knowledge

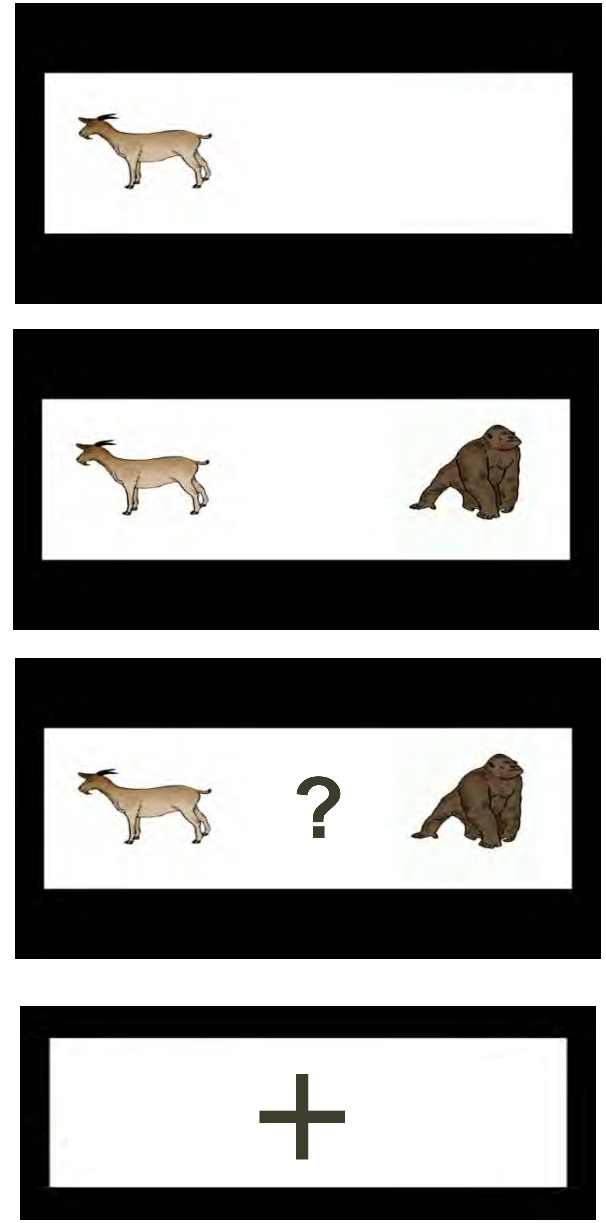
Psychophysics Measures:
- RAP (tones and environmental sounds)
- Rise Time perception

Questionaires :
- Development
- Home literacy
- SES

Tasks within MRI scanner :
- Phonological Processing
- Rapid auditory processing
- Executive functioning
- Reading Fluency

Structural brain differences (gray matter, DTI)





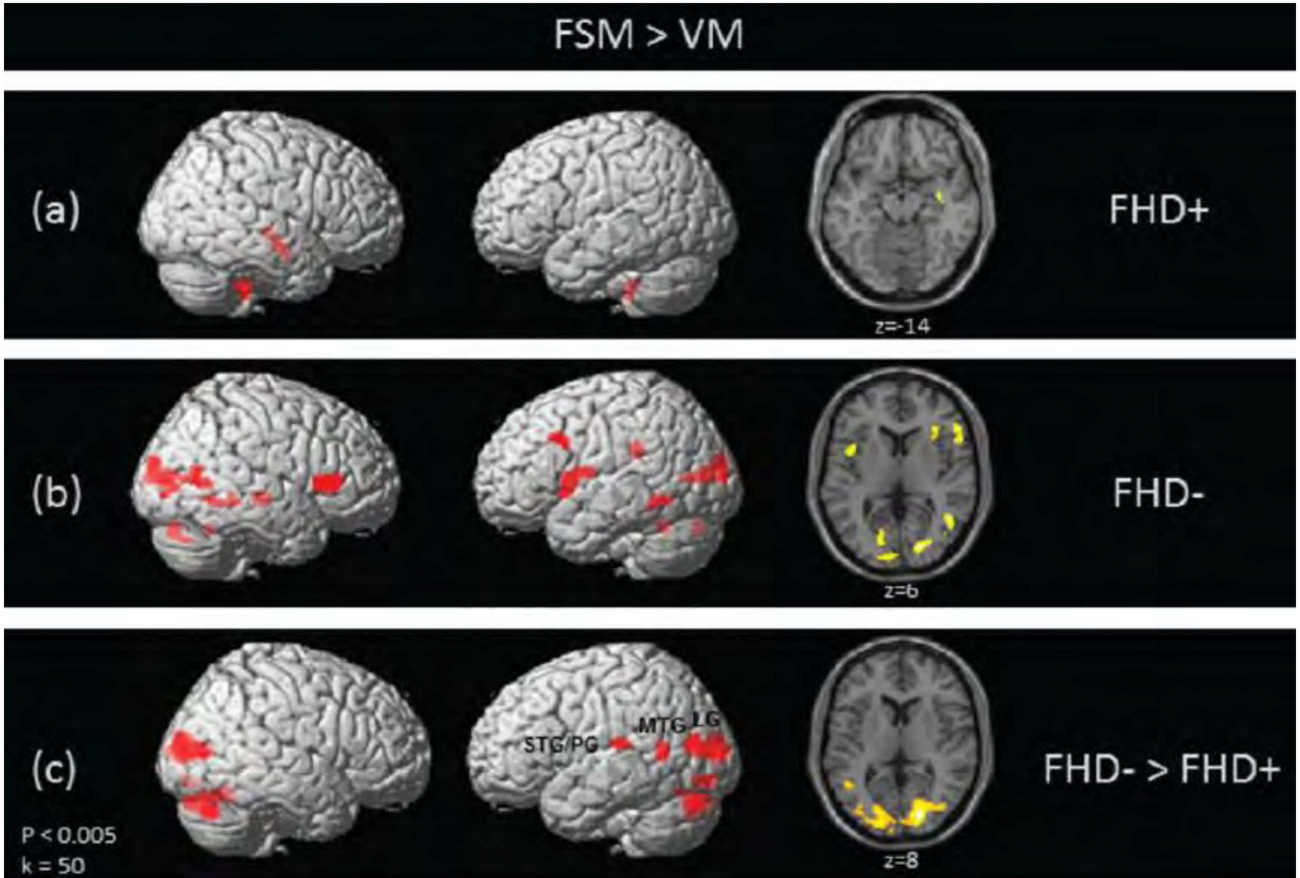
Control task:
Voice matching

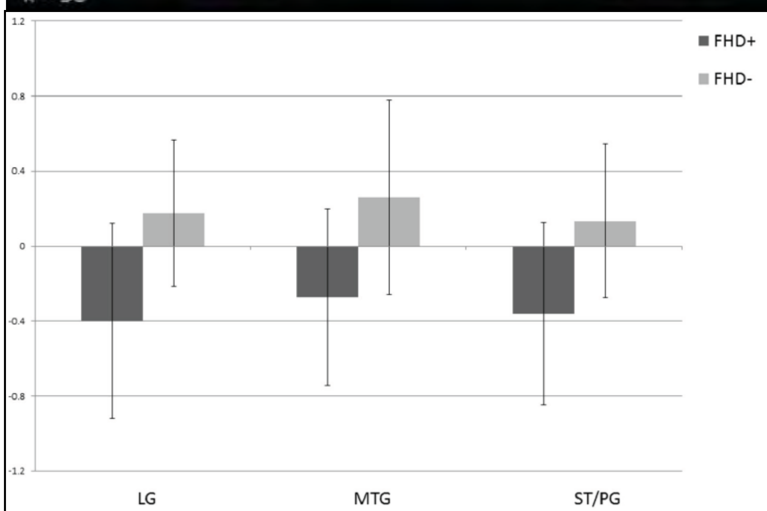
[Raschle *et al.*, 2009; Raschle *et al*., 2012]


1
2
3
Can you help them?

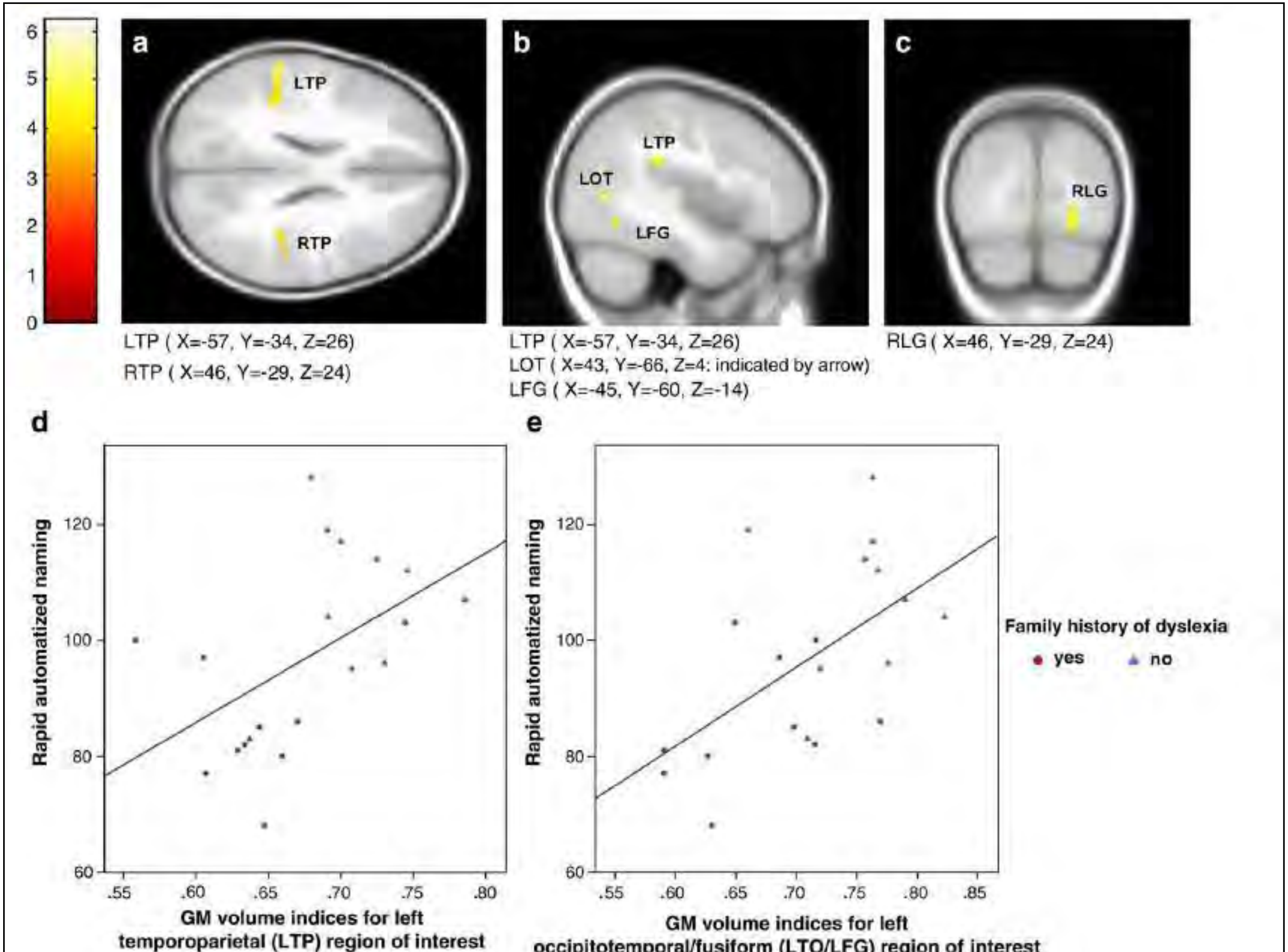
YEAR 1 (prereading status)	**YEAR 2 (beginning readers)**	**YEAR 3/4 (readers)**
Significant differences in:	*Significant differences in:*	*Significant differences in:*
Expressive and receptive language/content	Expressive language/ Language content	Core and receptive Language
Phonological processing	Phonological processing	
Rapid automatized naming	Rapid automatized naming	Rapid automatized naming
Rapid auditory Processing	Letter knowledge	
	Single word reading (timed/untimed)	Single word reading (timed/untimed)
	Passage comprehension	Passage comprehension
	Spelling	Spelling
		Reading Fluency
all $p<0.05$	*all $p<0.05$*	*all $p<0.05$*

No differences in
IQ, age, Home Literacy, SES





[Raschle *et al.*, PNAS 2012]



[Raschle *et al.*, 2010]

All left-hemispheric ROIs (Year 1) strongly correlate with reading skills in Year 2

Examining Genotype vs. Phenotype

Genotype

Based on familial risk

FHD+
- one 1st degree relative with a clinical diagnosis of DD

FHD-
- no relative with reading problems

Phenotype

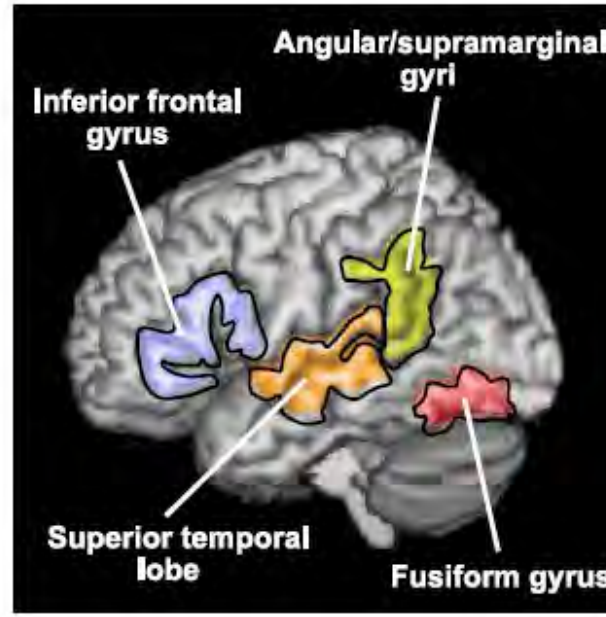
Based on reading scores after 1 year of reading instruction

PR
- TOWRE SWE average [SS]= 82.55

GR
- TOWRE SWE average [SS] = 109.83

Structural brain differences at the end of preschool based on reading scores (phenotype) one year later (VBM)

Good readers > Poor readers p<0.001unc



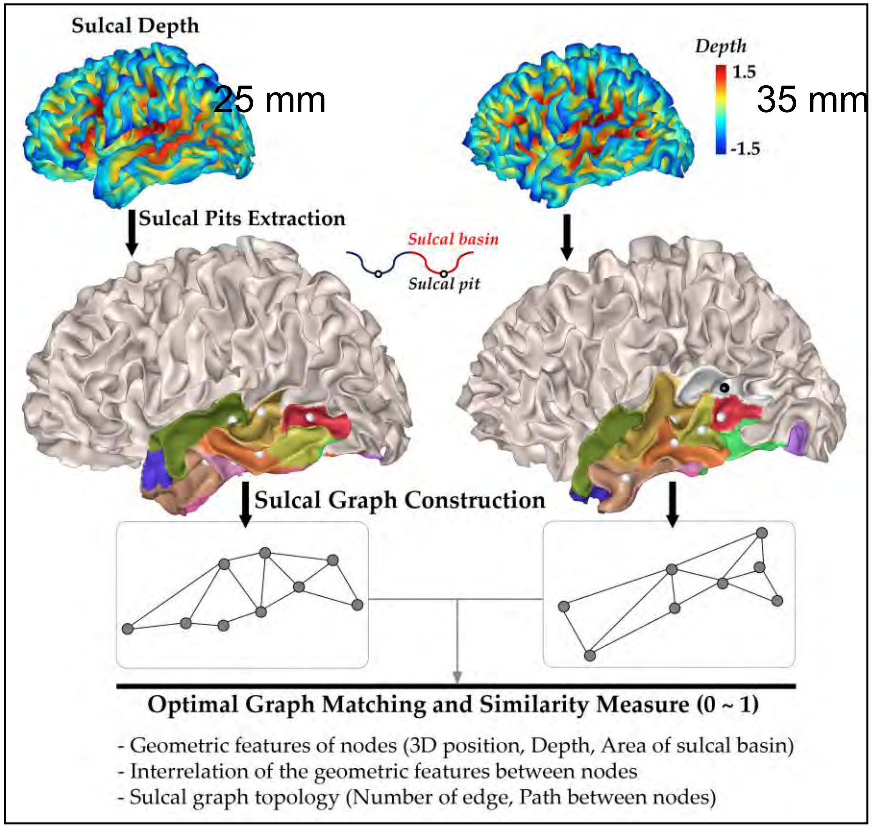
[Raschle *et al.*, in prep]

Bilateral atypical parietal sulcal pattern in pre-readers with familial risk of developmental dyslexia and young readers with developmental dyslexia

Im, K., Raschle, N., Smith, S., Grant, P.E. & Gaab, N. (under review)

- Sulcal pattern, meaning the global pattern of arrangement, number and size of sulcal segments, has been hypothesized to relate to optimal organization of cortical function and white matter connectivity (Van Essen, 1997; Klyachko and Stevens, 2003; O'Leary et al., 2007; Fischl et al., 2008), which cannot be examined with volumetric techniques.

- Individuals with DD may undergo atypical sulcal development originating from altered function and white matter organization. Moreover, global sulcal pattern is determined during prenatal development and may therefore better reflect genetic brain development (Rakic, 2004; Kostovic and Vasung, 2009).



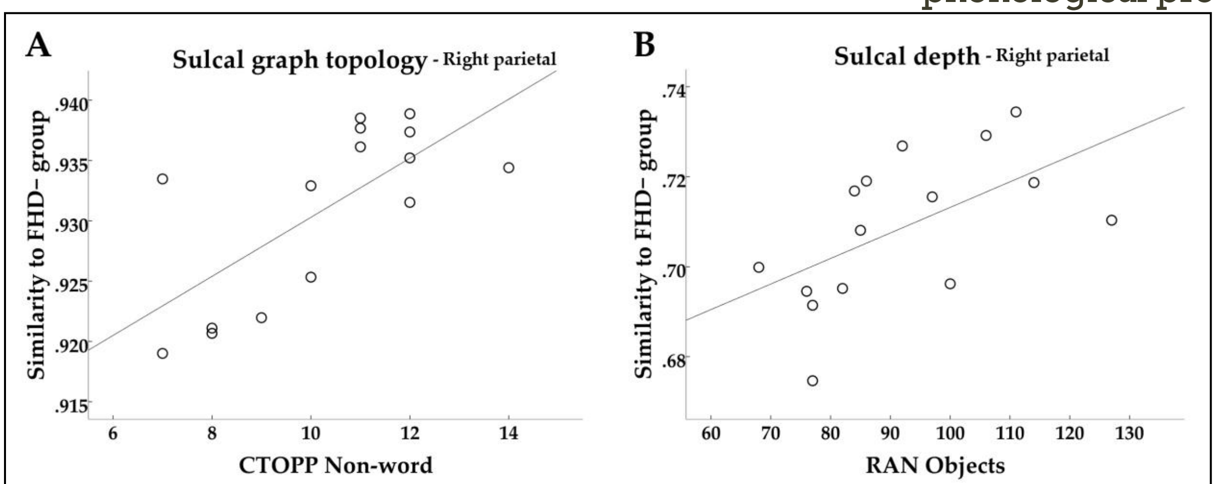
Four groups:

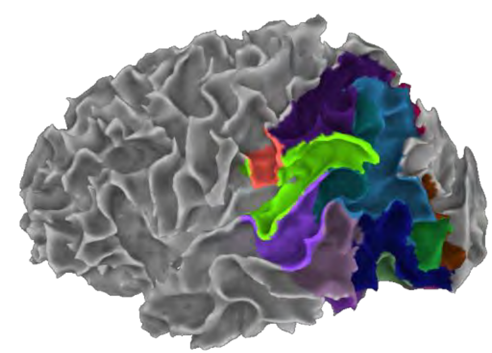
n = 16 Beginning readers FHD-
45 mm
n = 15 Beginning readers FHD+

n = 13 Developmental Dyslexia
n = 14 Typical developing

Bilateral parietal sulcal patterns atypical in pre-readers/beginning readers with a familial risk of DD compared to controls.

Significantly atypical bilateral parietal sulcal patterns were confirmed in children diagnosed with DD compared to controls, as well as its relationship with phonological processing and single word reading





Im *et al*., under review

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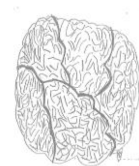
The READ Study

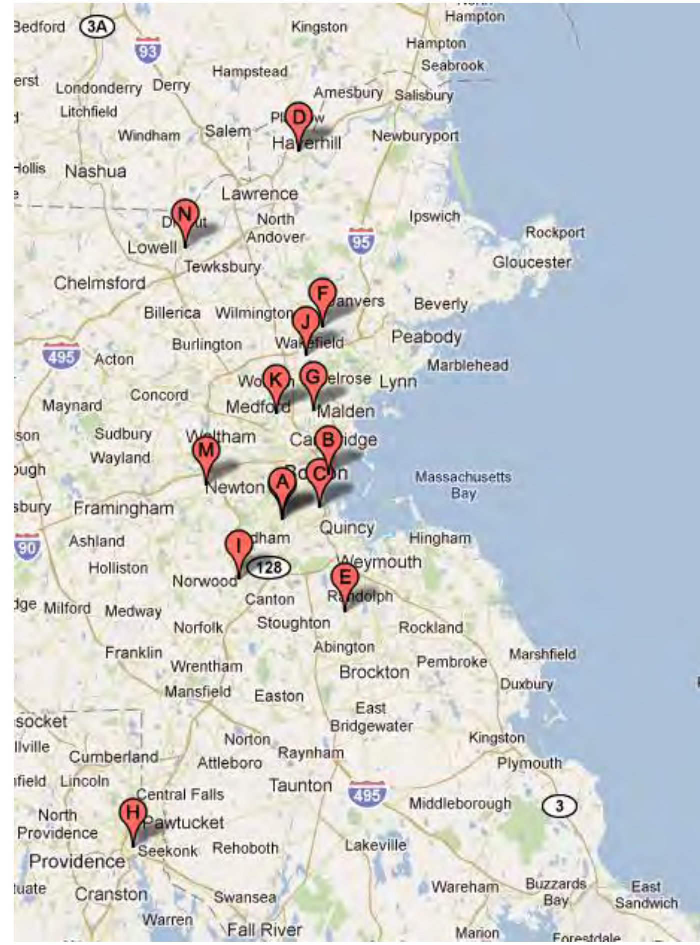
(Researching Early Attributes of Dyslexia)

- Screening over 1,000 kindergartners in New England with assessments known to predict reading outcomes and dyslexia in the fall of the 2011, 2012, and 2013 school years.
- To date 1,350 children in 21 ‘partner’ schools in New England tested so far in 2011, 2012 and 2013. Highly diverse sample in terms of SES, race/ethnicity, and school type.
- Inviting children with and without risk for dyslexia to participate in a follow-up study including brain imaging with MRI and EEG (to date n =180 for EEG and n=150 for MRI).
- Following these children to see which measures from kindergarten best predict reading ability at the end of 1st and 2nd grade.

READ at a Glance

- 21 schools: inner-city charter schools, private, suburban district-run schools, and Archdiocese schools
- Free/reduced lunch eligibility from 0% to 80%
- Ethnically diverse student population (49% minority)
- Teacher professional developments and parent presentations conducted in all schools
- Brain awareness days conducted in various schools





> *"We very much enjoyed everything you and your staff provided. You are warm and professional and certainly put your subjects at ease…It's exciting to see such cutting-edge research from the inside out!" (Parent, Wheeler School)*

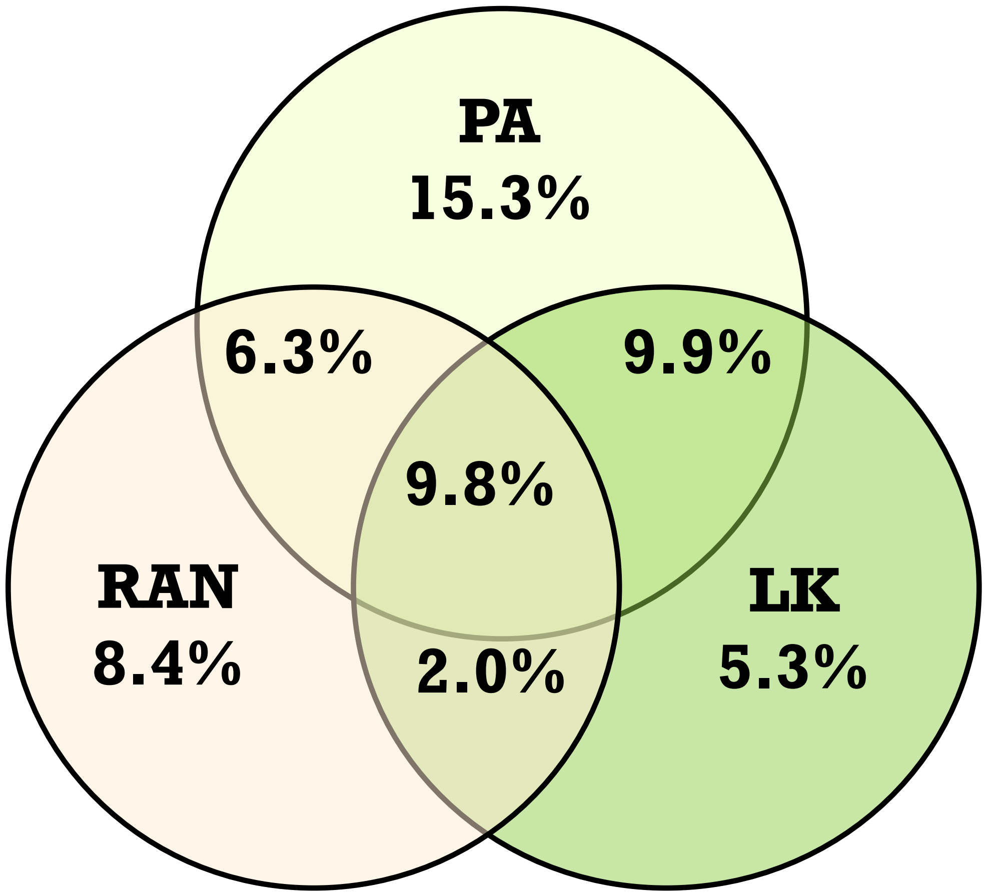
> *"…They were excellent presenters. The students had a wonderful time and were very engaged in the activities." (Teacher, Lowell Elementary)*

> *"Your whole team was terrific in making the afternoons lots of fun and educational" (Parent, Hosmer Elementary)*

Assessments

- Deficits in the following most consistently predict reading failures: phonological processing/awareness, rapid automatized naming abilities, and letter-name knowledge
- We will assess these with a 45 minute, individualized assessment
- Measures to be used include
  - Comprehensive Test of Phonological Processing (CTOPP)
    - –Elision
    - –Blending
    - –Nonword repetition
  - Woodcock Reading Mastery Tests (WRMT-III)
    - –Letter ID
    - –Word ID
  - Rapid Automatized Naming (RAN)
    - –Objects, Colors, Letters
  - KBIT Matrices

Subtypes of DD Risk: 25th Percentile Cutoff Based on Screening Sample

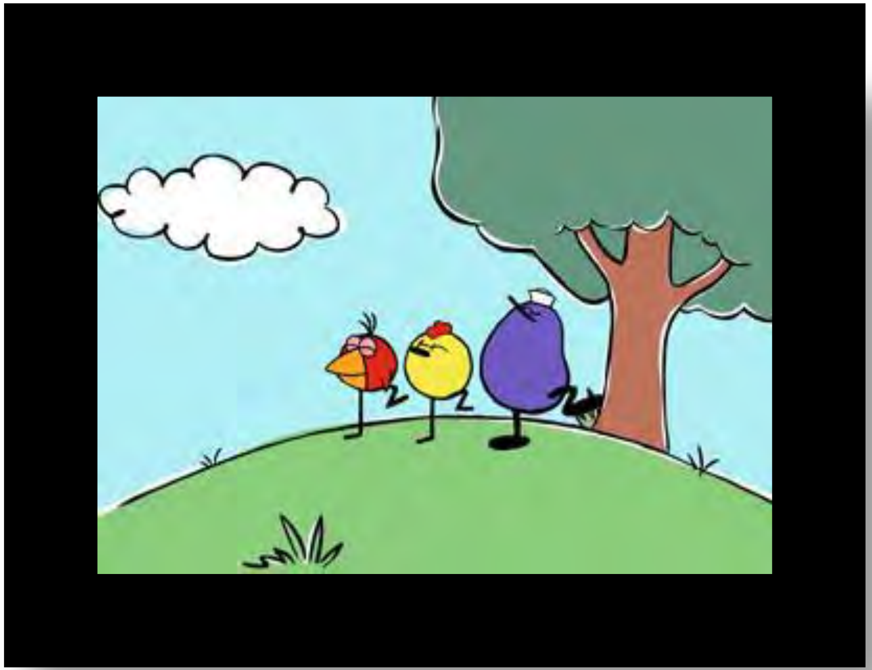


EEG: Electroencephalography

- We study the mismatch negativity (MMN)

→ a component of the event-related potential (ERP) to an odd stimulus in a sequence of stimuli. The MMN can be elicited regardless of whether the subject is paying attention to the sequence.

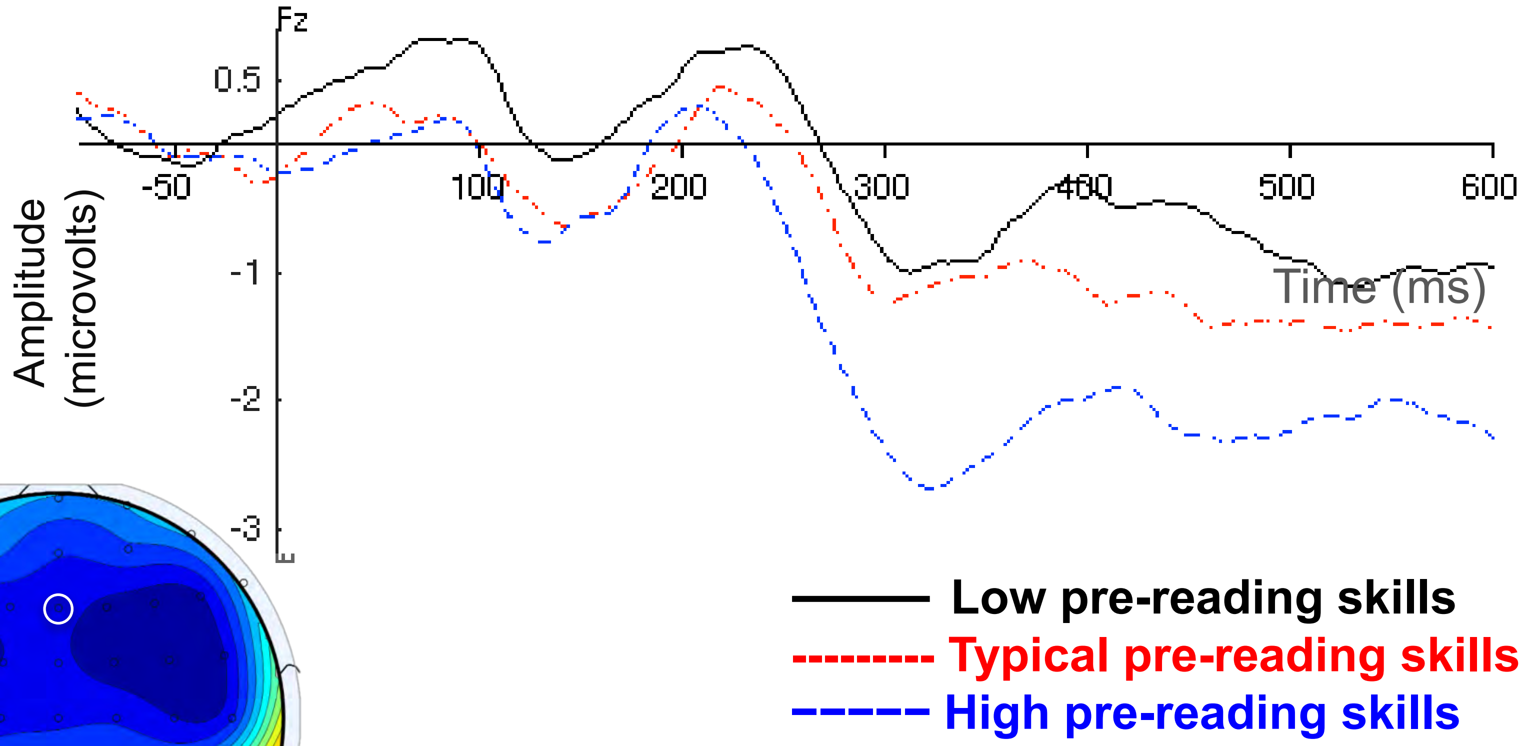
  - Auditory "oddball" – passive listening with no task

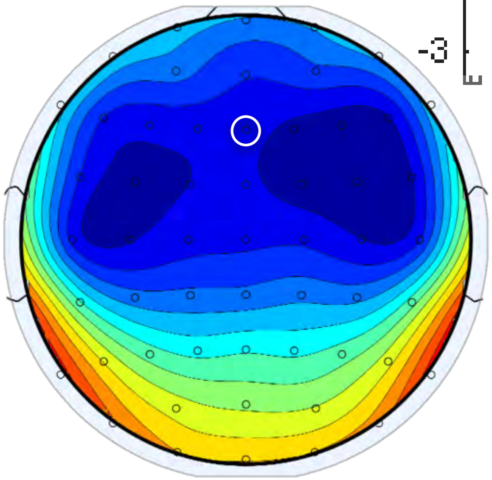


ERP MMN Data

Grand average MMN waveform (standard-deviant) at site Fz;

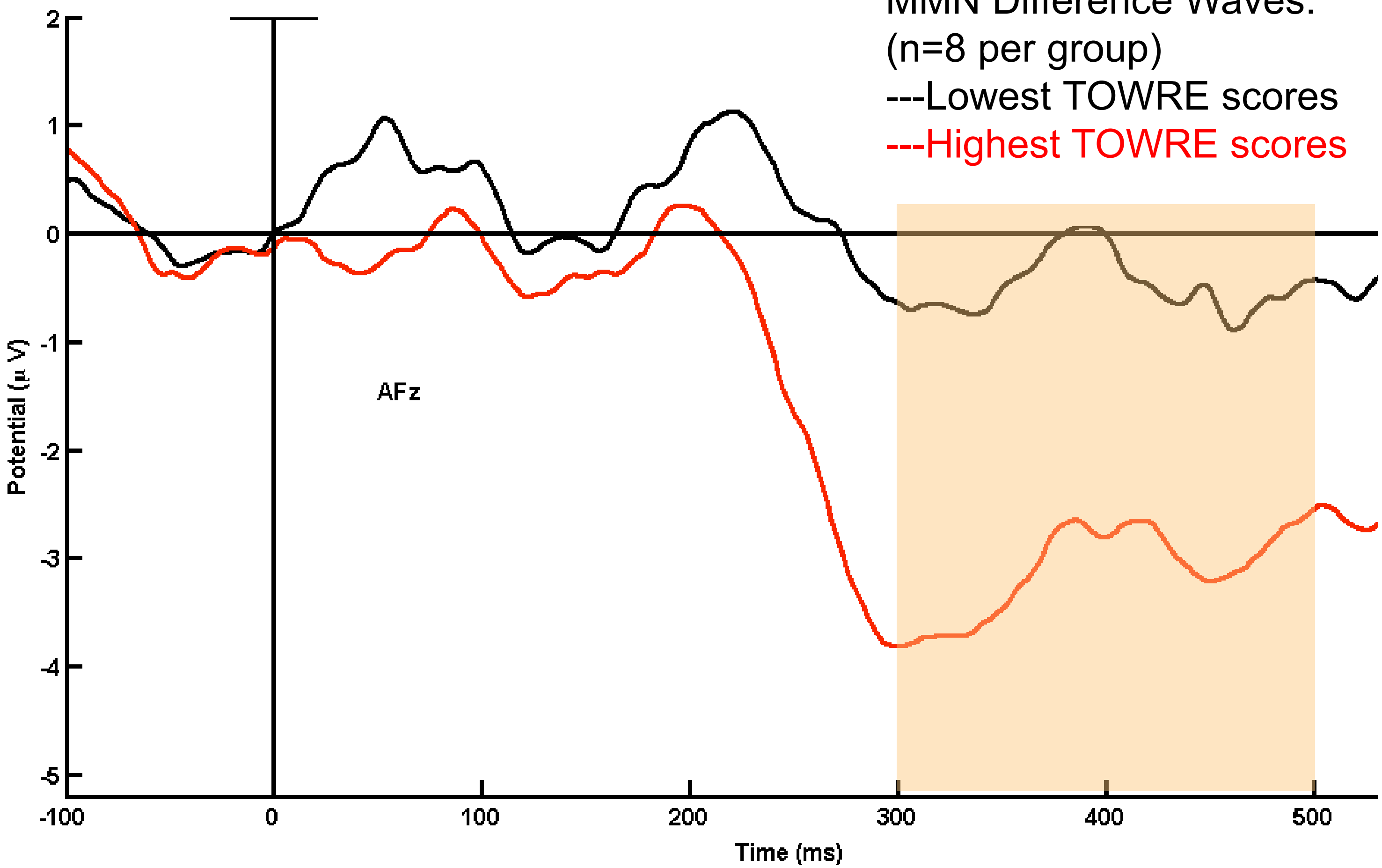
n=94





Norton *et al.*, in prep

Can kindergartners' MMN predict reading at the end of 1st grade?



MMN Difference Waves:
(n=8 per group)
---Lowest TOWRE scores
---Highest TOWRE scores

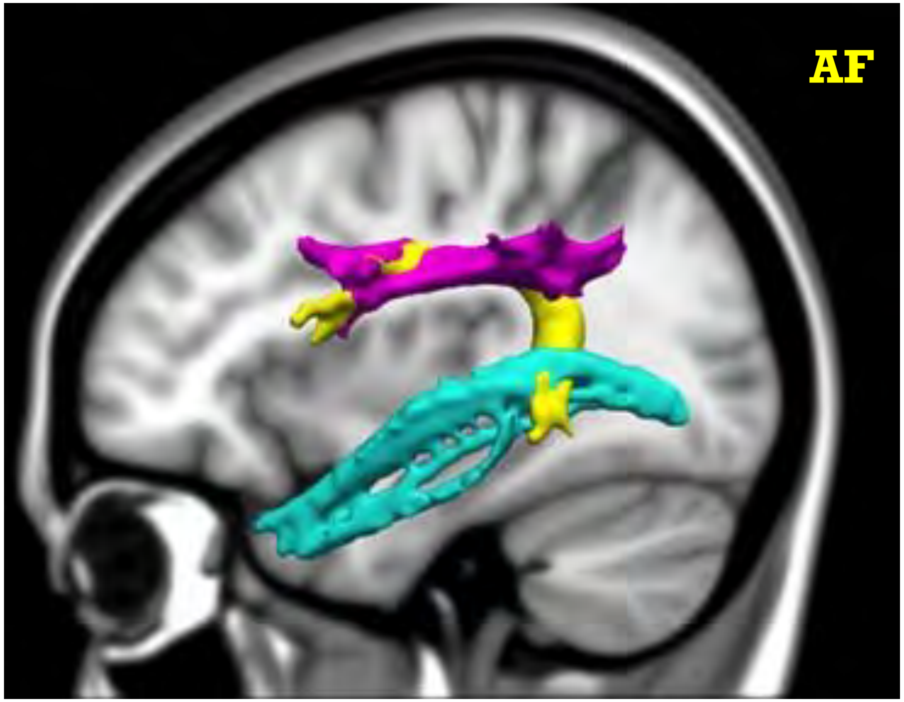
Mean amplitude 300-500ms differs between groups
p=.002

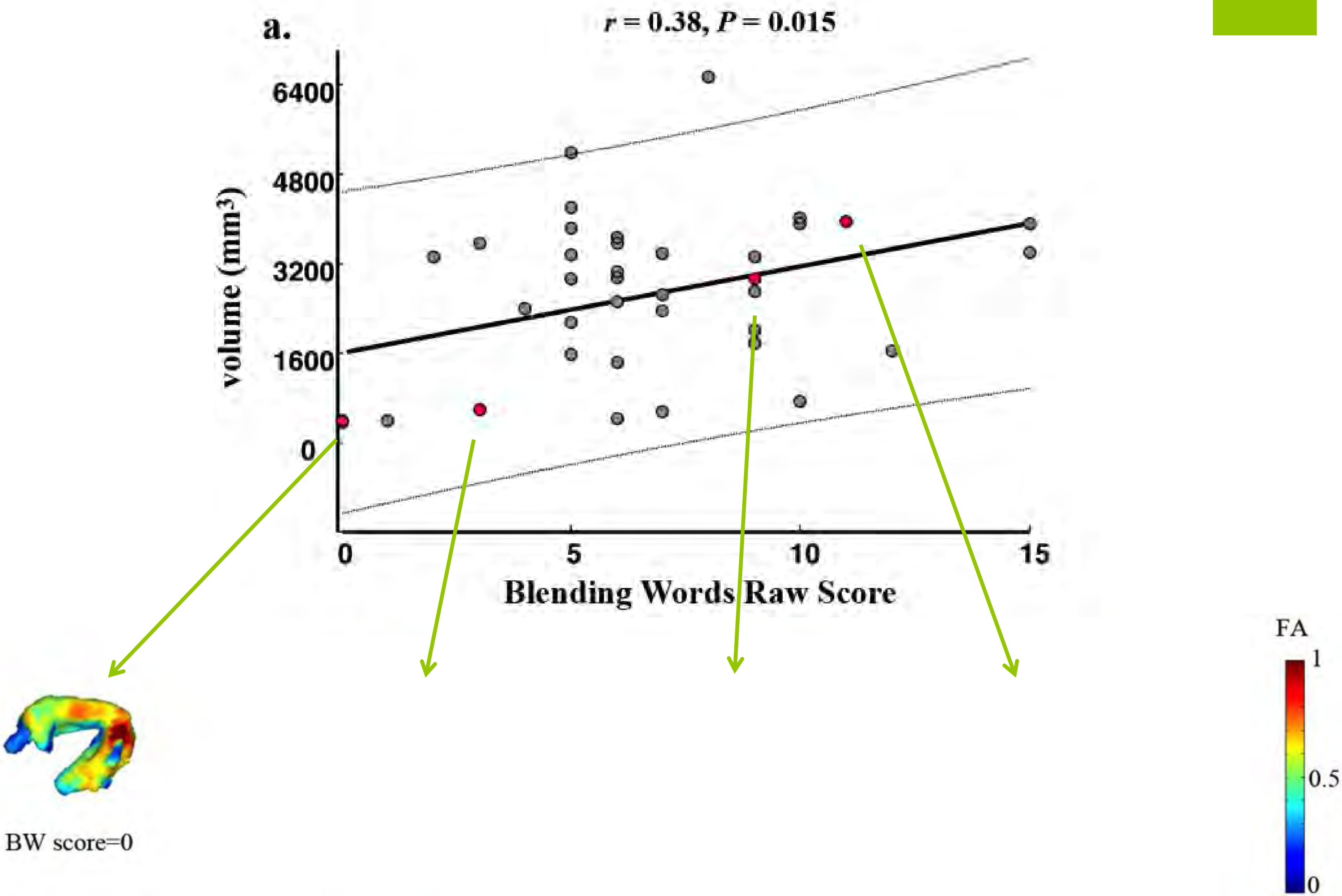
[Norton *et al.*; in preparation]

White matter in pre-readers

- The left arcuate fasciculus (AF) is a major white matter pathway connecting the brain's language areas.

- Are smaller volume and weaker organization of the AF in adults with dyslexia a cause or a consequence of poor reading?





Saygin, Norton *et al.*, J Neurosci 2013

Summary for READ

- In the present study, we demonstrate that previously described white matter alterations in DD already exist in preschoolers/kindergarteners with behavioral risk for DD.

- Patterns of hypoactivation/attenuated MMNs in key brain regions seem to differ depending on risk subtype suggesting differences in the underlying mechanisms.

- Children at risk in RAN have attenuated MMN relative to children not at risk or at risk in PA or LK suggesting that MMN may be an index of the automaticity shared with the processes that underlie efficient naming and reading tapped by RAN.

Overview

- Overview about the Brain
- The typical and atypical reading brain
- Remediating the reading brain
- Can brain measures enhance the accurate identification of children at risk for DD?
    - The Boston Longitudinal Dyslexia Study (BOLD).
    - Project READ (Research on the Early Attributes of Dyslexia)
- Detecting children at risk for DD in infancy?
- Educational and Clinical Implications

Demographics

	FHD-	FHD+	T-test 2-tailed
N	14	14	
Age (days)	316.57 ± 100.55	289.14 ± 115.95	p > .100
Expressive Mullen T-score	48.67 ± 4.77	47.90 ± 10.87	p > .100

OPEN ACCESS Freely available online

PLOS ONE

Tract Profiles of White Matter Properties: Automating Fiber-Tract Quantification

Jason D. Yeatman[1,2]*, Robert F. Dougherty[2], Nathaniel J. Myall[3], Brian A. Wandell[1,2], Heidi M. Feldman[3,4]

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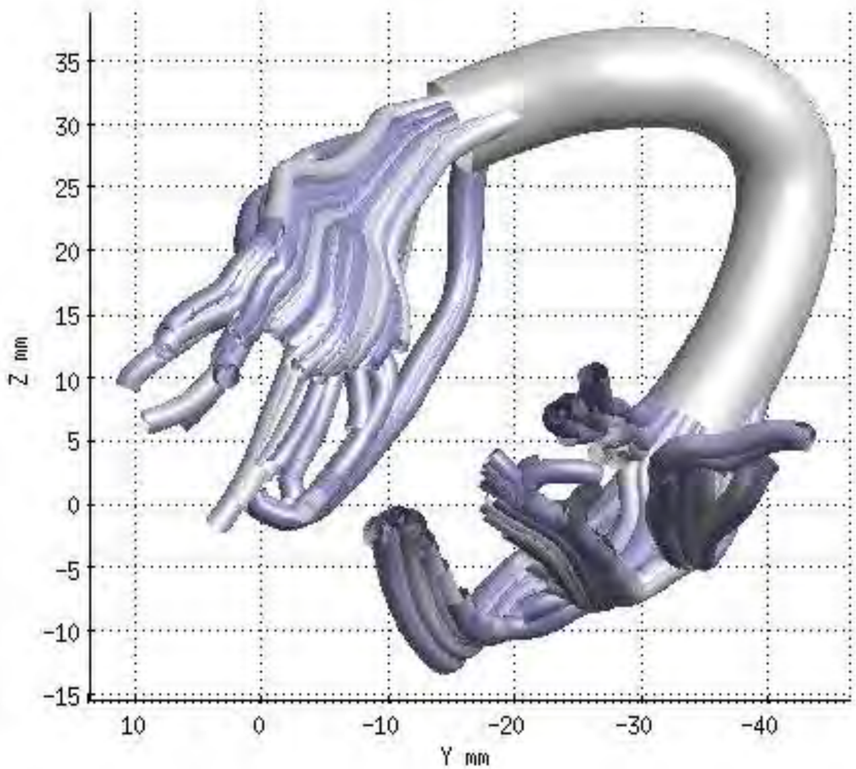
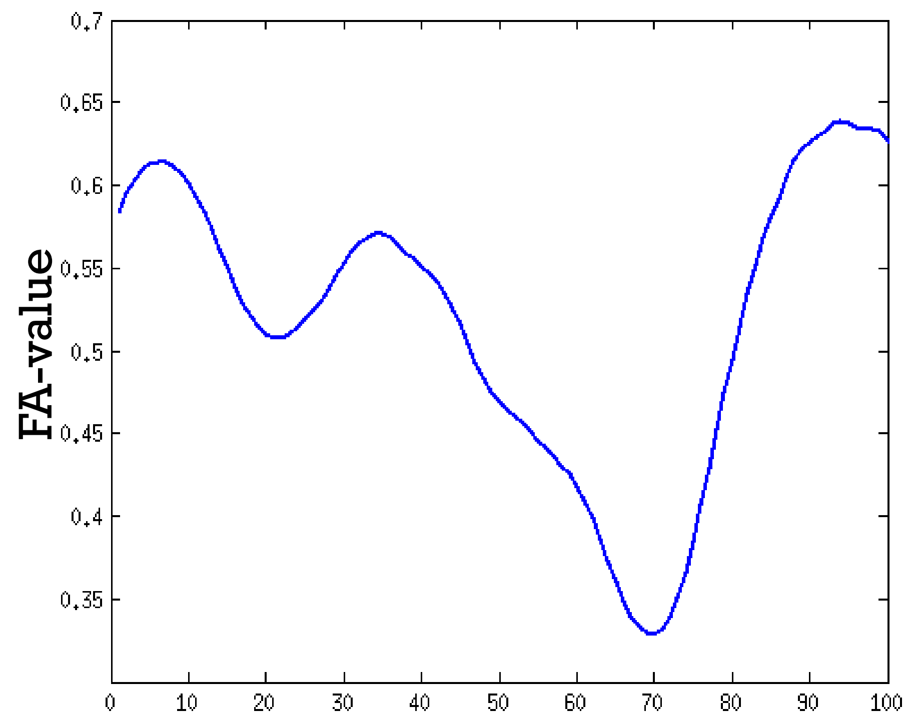
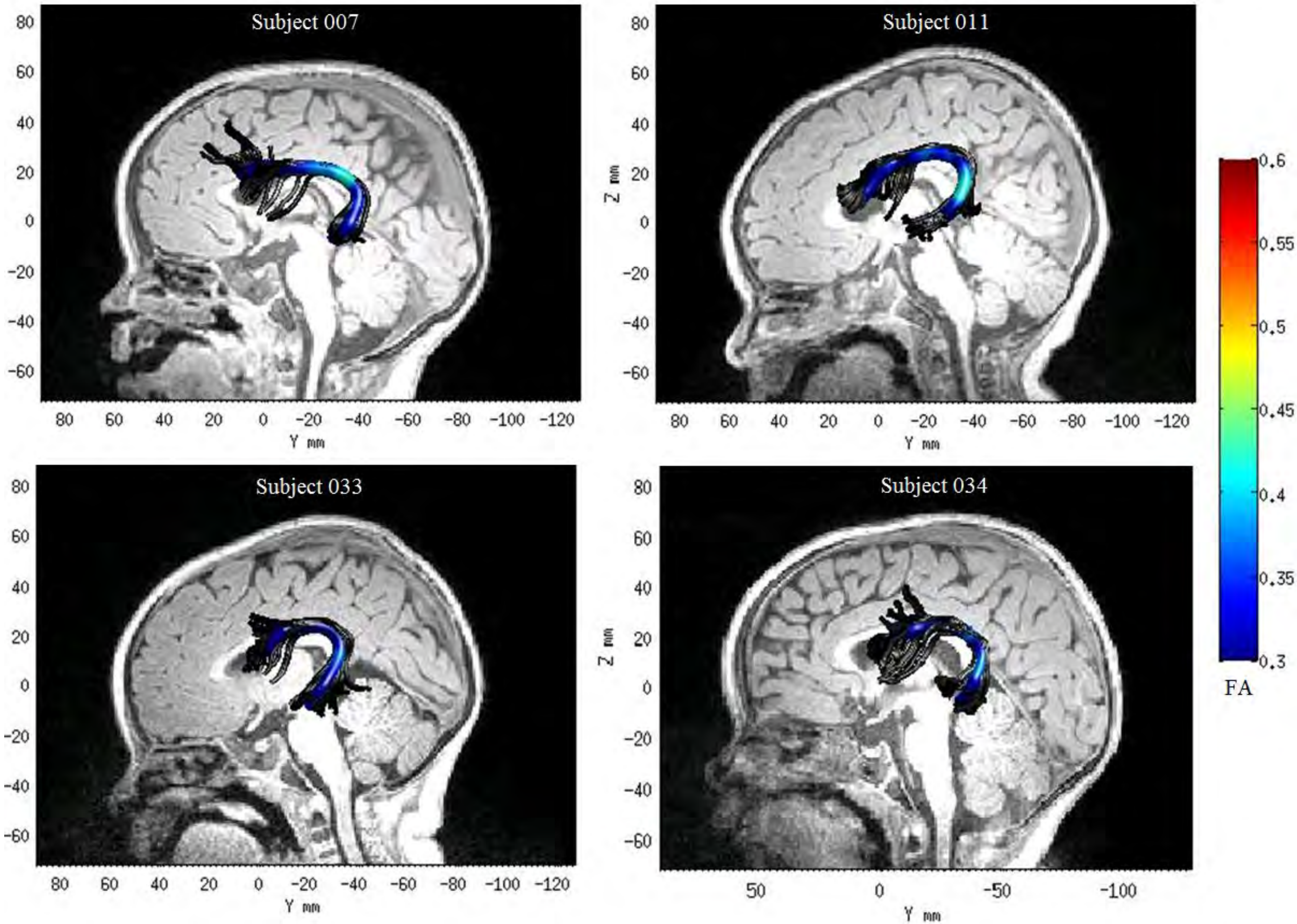
Tract Diffusion Profile





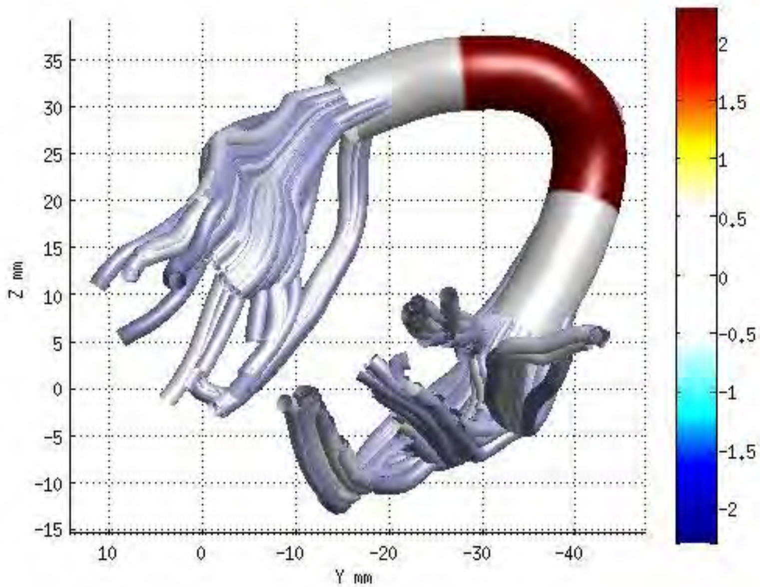
location on the tract

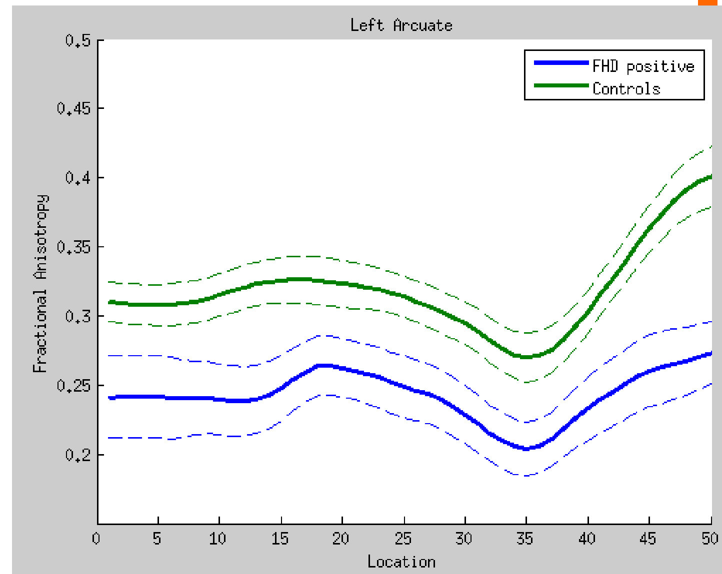
AFQ



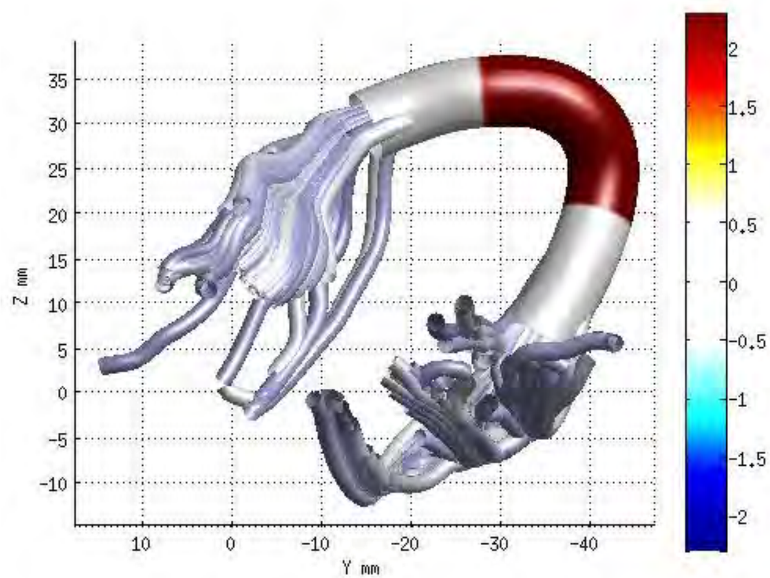
Subject 007
Subject 011
Subject 033
Subject 034
Y mm
Z mm
FA
0.6
0.55
0.5
0.45
0.4
0.35
0.3

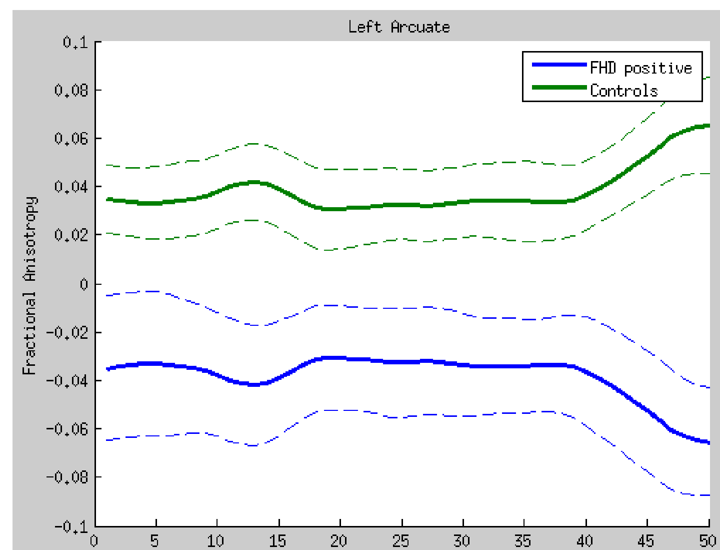
LH Arcuate FA Comparison (*p*-values range from 0.05 to 0.0004)





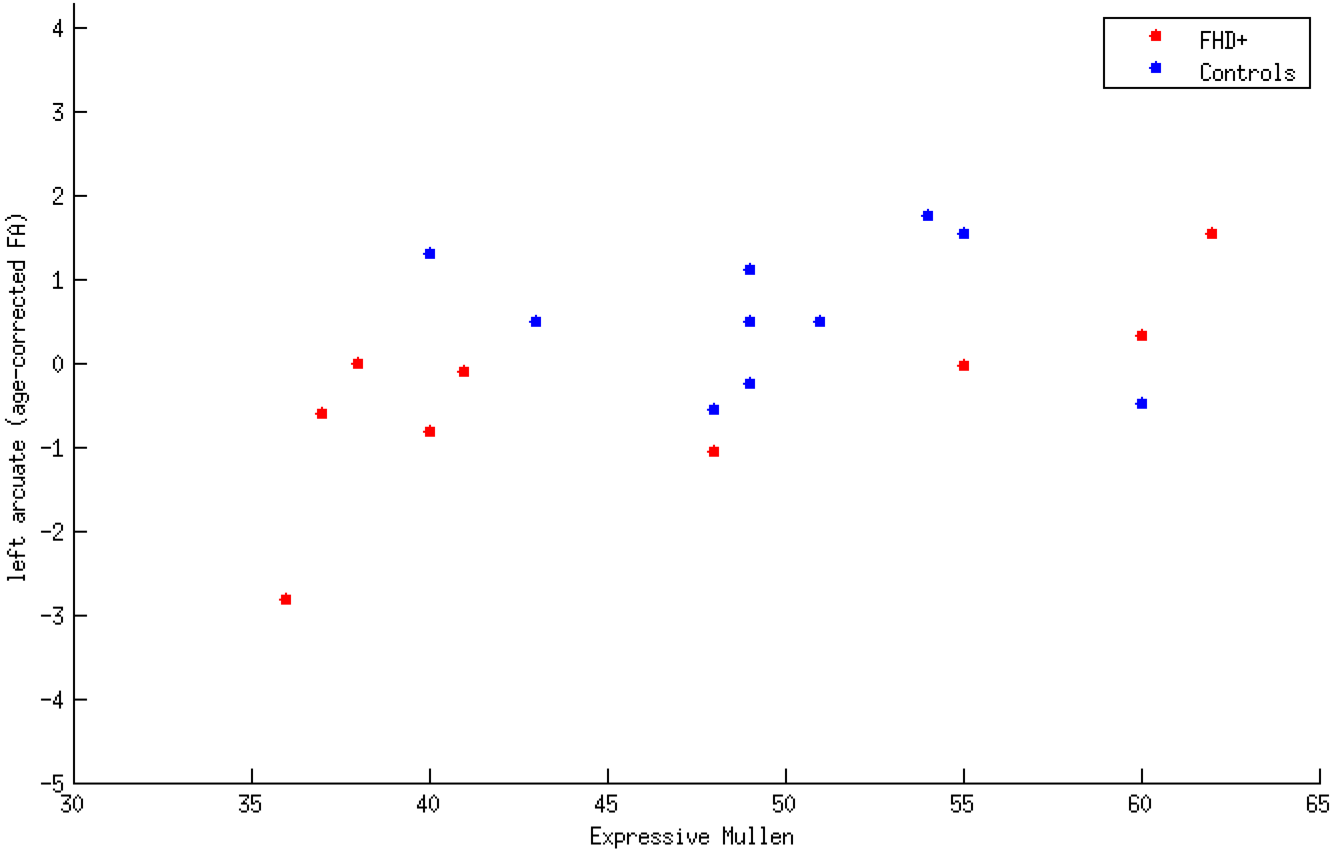
LH Arcuate FA Comparison age-corrected (*p*-values range from 0.05 to 0.0002)





Langer *et al.*, in prep

FA values correlate with Expressive Language Scores



R = 0.481
p = 0.037

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Educational and Clinical Implications

- Early identification may reduce the clinical, psychological and social implications of DD.
- Development and implementation of early and customized remediation programs
- Changes in educational policies (early IEPs; design and implementation of customized curriculums for children at-risk).
- Evaluation and improvement of existing remediation programs will likely prove cost-efficient as programs are made more effective.
- Improved psycho-social development (reduced child stress, parental stress, improved overall family dynamic).
- Maximizing use of ‘intellectual potential’.
- Most importantly, maximizing the joy to learn to read.

Other projects in the GaabLab

- Examining the comorbid brain (DD/ADHD): two distinct disorders?
- Time- and cost-efficiency analyses for psychometric/fMRI data
- Neural correlates of reading fluency in typical and atypical readers
- Examining the link between musical training and cognitive/language development
- Music as a diagnostic or intervention tool? [Brazil Project]
- Dyslexia in Fetal Alcohol Syndrome (with Joseph/Sandra Jacobson: Cape Town)
- Autism (BCH site investigator for NIH Autism Center Excellence Program)
- The delayed development of implicatures: inferences from fMRI (with Gennaro Chierchia, Harvard University)

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April Benasich, Rutgers University
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Gennaro Chierchia, Harvard University
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Michelle Lee (Psychometric Assessments)
Sarah Beach (RA, READ)
Abby Cyr (RA, READ)
Zeynep Saygin (READ)
MRI Team, Children's Hospital Boston & MIT

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- Harvard Catalyst (Infants)
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- Charles H. Hood Foundation (BOLD)
- Grammy Foundation
- William Randolph Hearst Foundation (Infants)
- Children's Hospital Boston Pilot Award (BOLD)
- Developmental Medicine Center Young investigator Award
- Victory Foundation

www.childrenshospital.org/research-and-innovation/research-labs/gaab-laboratory
www.babymri.org